8.6 Physician Adjudication

A WHI Extension Study outcome is adjudicated by assigning the appropriate outcome diagnosis based on Extension Study-defined criteria for each condition and recording clinical and supporting diagnostic information on an outcomes form.

The Physician Adjudicator has the responsibility for making all final assignments of diagnoses in the adjudication process and signing each outcome form indicating that he or she has completed or has overseen the diagnostic decision-making and agrees with the final diagnosis. Physicians doing adjudication must be familiar with general internal medicine principles, and in particular, with the diagnostic work-up of cardiovascular disease (CVD), strokes, and fractures.

The Physician Adjudicator is to be blinded to randomized treatment assignment in CT cases and to exposure status in OS cases. While CT participants were formally unblinded at the end of each CT component, having knowledge of this information when adjudicating a WHI Extension Study case may bias the adjudication decisions.

8.6.1 Physician Adjudicator Training

Before attempting outcomes adjudication, the Physician Adjudicator must complete a training process which includes the following:

Central Training:

- Participation either in adjudication training discussions at WHI Extension Study meetings or on a Physician Adjudicator training conference call Physician Adjudicators may participate in both, if desired.
- Participation in the mentoring program whereby a new Physician Adjudicator is paired with an active centrally trained adjudicator who is familiar with WHI adjudication and WHI Extension Study procedures. This pairing targets a Physician Adjudicator who has not been a central adjudicator before.
- Additional training through the feedback provided from central adjudication of the outcomes of interest, at selected regional meetings, at the annual general meeting, or on the Outcomes Adjudication Committee (OAC).

Reading:

- *Section 8 – Outcomes.*
- For physicians not currently familiar with reading electrocardiograms (ECGs), the following reading may be helpful:
    - Crow, R.S., Prineas, R.J., Jacobs, D.R., et al. (1989). A new epidemiologic classification system for interim myocardial infarction serial electrocardiographic changes. *American Journal of Cardiology*, 64:454-461.
    - Dubin, D. (1996). Rapid Interpretation of EKG's, 5th Ed. Tampa, Florida, Cover Publishing Co.
    - Goldschlager, N., and Goldman, M.J., (1989) *Principles of Clinical Electrocardiography*, 3rd ed. Norwalk, CT: Appleton and Lange.

8.6.2 Adjudication Overview

For the WHI Extension Study, WHI moved from a two tiered, local and central adjudication model to a single centralized adjudication process. FC staff route all outcomes to the CCC, which then distributes the cases to Physician Adjudicators or other CCC resources.

Each Physician Adjudicator who receives the FC prepared adjudication case reviews it and takes the following steps:

- Review the case packet to ensure all required documents are present.
  - Request additional documentation, as needed. (For the current outcome under investigation or a discovered event not self-reported by the participant.)
- Confirm or deny the outcome by reviewing the case packet documents and completing the appropriate outcomes forms.
  - Notify the CCC if any case packets should be merged.
  - Complete forms for any additional outcomes identified from the medical records.
- Complete specific reports, such as Investigation Documentation Summary.
- Return the case packet and completed documents to the CCC within 2 weeks of receipt.
  - Request routing to additional committees for adjudication if required.
  - Request review, by Full Committee.

8.6.3 Review the Adjudication Case Packet

When reviewing the adjudication case packet, the Physician Adjudicator will decide, for each outcome, whether the relevant medical records documents are present (see *Table 8.2 – Required Documents for Outcomes)*. For all outcomes involving a hospitalization, this documentation will include, at the minimum, a hospital Face Sheet, and/or Physician Attestation Sheet (including admit and discharge dates, discharge diagnoses, and, usually, ICD-9-CMor ICD-10 CM codes for each discharge diagnosis and procedure). Most hospitalized outcomes also require a hospital Discharge Summary, which will include admitting signs and symptoms, initial impressions, hospital course, procedures, and final discharge diagnoses. If all required documentation is present (including those possible WHI Extension Study outcomes identified in the medical records but not reported by the participant), the Physician Adjudicator may proceed in assigning a diagnosis by completing the appropriate outcomes form.

8.6.3.1 Contents of the Case Packet

The adjudication case packet consists of the following documents:

- *Members Outcomes Status Report* (MOSR), (*WHIX1215*), which provides individual participant information about confirmed outcomes, outstanding outcomes that have not yet been assigned to the Physician Adjudicator, and pending adjudications. Randomization/enrollment status is also listed. This information is helpful when determining first vs. subsequent outcomes; when determining if adjudication cases should be "merged" because they refer to the same event (e.g., specific cancer diagnosis or fracture treatment); and identification of HT participants requiring additional outcomes forms.

- *Investigation Documentation Summary* (IDS), *(WHIX0988*), lists specific information about the adjudication case packet documents. Based on the participant's self-report, the provider visits for which medical records have been requested is summarized. The name of the medical providers and dates of service are reported, along with the list of medical records requested and the status of each request (i.e., the document was received, not available or a substitute document included). The OC may type comments about the status of the medical record documents on this report. The Physician Adjudicator is required to complete the IDS for each adjudication case reviewed.

- *Adjudication Rules Report (WHIX1001)*. This "optional" report indicates the study or studies to which a participant is randomized or enrolled, the date of CT randomization or OS enrollment, and the date of her CaD randomization, if any. The report lists confirmed outcomes (excluding hospitalization-only cases) with the date of the latest confirmed diagnosis and those outcomes that still require adjudication. When manually updated by the OC, the report also takes into account the subsequent condition rules (see *Table 8.3 – Subsequent Conditions*). By default, the "adjudication required" flag for each outcome type is typically set to "yes" (i.e., requires adjudication). Exceptions to the default parameter include: hysterectomy, PE, and DVT for non-HT participants, which are automatically set to "no".

- *Documentation*. Medical records documentation, should be consistent with the required documentation sets identified in *Table 8.2 – Required Documents for Outcomes*. Appropriate explanations should be listed on the IDS if medical records are missing or additional medical documents are included.

- *Outcomes Forms*. Outcomes forms, as listed in *Table 8.6 – Required Adjudication Forms*. Note that the Physician Adjudicator should have an additional supply of outcomes forms in case additional outcomes are found during the adjudication. If the adjudication case requires review by another committee, indicate this by selecting the appropriate box on the IDS report.

8.6.3.2 Incomplete Adjudication Case Packets

If the Physician Adjudicator judges the adjudication case packet to be incomplete, s/he should return it to the CCC along with a request for the additional documentation. The CCC will forward the query for the additional documents to the FC. There may be instances when the FC cannot get complete documentation. In these cases, the Physician Adjudicator should proceed with assigning a diagnosis using the available documents.

The OAC developed an Extension Study Query Process document to provide guidelines for when a query is generated by the Physician or CCC Adjudicator and instructions for how to process a query for a discovered event and/or a missing document.

Physician Adjudicators

a. Missing medical records documentation

Generate a query for a case missing one or more essential documents, i.e., those documents required to appropriately classify the outcome. On rare occasions, a non-essential document may be needed to complete the adjudication.

b. Terms/conditions for which a query would not be generated

- A "remote" history of an outcome
- No date of service provided or date of service is *before* April 1, 2005
- An outcome diagnosed "last year" or "last summer" w/o mention of date.
- Non-cancer outcomes: any future diagnostic test/work-up to diagnose a non-cancer outcome (e.g., hip fracture, stroke, or heart attack). (**Note:** Cancer queries are generated for future diagnostic workup when related to the initial cancer diagnosis.)

c. Discovered events

Restrict queries for *discovered* events to the following outcomes:

- MI
- Stroke
- Hip fracture
- Death
- Cancer (primary and other cancers [excludes non-melanoma skin cancer])
- DVT/PE (HT only)

If a 'discovered event' i.e., an unreported outcome is identified in the medical records and you are unsure if it has been investigated, or an essential document is missing from the case under current review, check the 'add'l documents needed' box on the Investigation Documentation Summary (IDS) and document a query, i.e., for the discovered event or missing document. The Outcomes Unit will follow up on the query.

CCC Adjudicators (Hospital/Cancer Committee)

Initiate a query if you identify a primary WHI outcome with documented dates of service and the outcome was not previously reported on the following WHI forms:

- WHIX1215 – Members Outcomes Status Report (MOSR), closed and pending cases
- WHIX: *Form 2/3* and *Form 30* baseline forms

Outcome Coordinators – Instructions for Processing Queries

a. A *discovered event* is an additional provider visit and/or outcome condition identified by the adjudicator in the current set of medical records. It is typically not related to the case under review (cancer is an exception) and must be *diagnosed on or after April 1, 2005*.

Action: Procure the required medical records from the health care provider which may require obtaining a new Release of Information (ROI) from the participant. Assemble the new adjudication case per Extension Study procedures. Attach the original CCC query to the case and forward to the CCC as part of your next CCC FedEx shipment.

WHIX: Manually create a new condition (if necessary), provider visit, and adjudication case rather than inserting the new documents into the current case under CCC review.

b. A *missing document* query is generated when a required document is not present in the current case review and is needed to accurately classify the outcome of interest.

Action: First check to see if the missing document is in the participant's FC file. If not, obtain the required document from the health care provider which may require obtaining a new Release of Information (ROI) from the participant. File a copy of the document in the FC case. Route the original document (blacked out) and a copy of the original CCC query to the CCC for inclusion into the case.

WHIX: Insert each document as "1-received" in the Provider Visit Documents screen and enter notations in the Comments Column when appropriate.

8.6.4 Assign a Diagnosis and Complete the Outcomes Forms

The adjudicator should read through the entire adjudication case packet including the medical documents and WHIX reports carefully, particularly the face sheet and discharge summary. Be aware that more than one outcome may be present in a packet, even though the *Investigation Documentation Summary* (WHIX0988) may not reflect this. Thus, all documents in a case packet, including those hospitalizations that are not thought to include outcomes, should be reviewed for possible outcomes.

Complete the appropriate outcomes adjudication forms: See *Table 8.6 – Required Adjudication Forms* for a list of the forms to complete for each type of case. The outcomes forms must include sufficient information (e.g., participant ID) to ensure they do not get mixed up with other cases. Refer to *Sections 8.7 - 8.10* for specific instructions for completing the forms. In general, only **one** outcome form is completed for each outcome being investigated.

8.6.4.1 Hospital Stays

Any case packet that includes a hospital stay of 2 nights or more, or a one night stay for selected outcomes, will include a completed *Form 125 – Summary of Hospitalization Diagnosis*. Note that some procedures, even if they result in a hospital stay of 2 nights or more may not require completion of a *Form 125*. Refer to *Section 8.2.1.2 – Outcomes Identified Only by Self-Report of Form 33/33D*.

The FC OC is responsible for transcribing and data entering the codes on to *Form 125*. Note that ICD-9-CM or IDC-10-CM codes should **not** be corrected or added (even if the Physician Adjudicator disagrees with a code as listed) but instead should be transcribed as they appear on the medical records document.

8.6.4.2 Merging Case Packets

Merge case packets, when appropriate. The Physician Adjudicator may receive more than one case packet for a participant whose total documentation (e.g., diagnosis and treatment of one event) indicates only one outcome. If this occurs, combine the case packets into one adjudication case with one outcome form. This is referred to as "merging" cases, and is allowed for the following scenarios:

- Inter-hospital transfer
- Intra-hospital transfer
- Cancer diagnosis, e.g., outpatient biopsy followed by tumor removal in hospital or at day-surgery
- Fracture diagnosis, e.g., X-ray at one facility followed by treatment at a different facility

Note that cardiovascular visits are adjudicated separately unless they are an inter- or intra-hospital transfer (i.e., a direct transfer on the same day).

Refer to the appropriate sections in this manual for more detailed information on the diagnostic criteria for WHI Extension Study outcomes.

Table 8.6
Required Adjudication Forms

Outcomes		Required Forms
Deaths	Due to CHD (Coronary death)	
	In hospital	(120), 121, 124, 125
	Out of hospital	(120), 124
	All other	
	In hospital	(120), 124, 125
	Out of hospital	(120), 124
Cardiovascular	(Hospitalizations unless otherwise noted)	
	MI	121, 125
	Stroke (in and out patient)	132, (125)
	Peripheral arterial disease (PAD)	121, 125
	Carotid artery disease (CAD)	121, 132, 125
	Coronary revascularization procedures (in and out patient)	121, (125)
	Coronary death (in and out patient)	121, (125)
Cancers	Breast, endometrium, ovary, colon, rectum, all other cancers	
	In hospital	130, 125
	Out of hospital	130
Hip Fractures	In hospital	123, 125
	Out of hospital	123
Hospital stay of 2 nights or more	(and one night stays for select outcomes)	125
HT only	**Venous thromboembolic disease (DVT/PE)**	
	In hospital	126, 125
	Out of hospital (DVT only)	126
	Hysterectomy	
	In hospital	131, 125
	Out of hospital	131

Form 120 – Initial Notification of Death. Completed by FC or CCC staff.

Form 121 – Report of Cardiovascular Outcome. Diagnosis of cardiovascular outcomes, including MI, coronary death, carotid artery disease, peripheral arterial disease, and coronary revascularization, (i.e., CABG and PTCA), but excluding stroke and transient ischemic attack (TIA). Only events requiring hospitalization or occurring **during** a hospitalization for another reason (except coronary death and coronary revascularization procedures) are counted as cardiovascular outcomes.

Form 123 – Report of Fracture Outcome. Any occurrence of a hip fracture. All other fractures are collected on *Form 33* by self-report.

Form 124 – Final Report of Death. Final cause of death. For hospitalized deaths, this will usually be when the Discharge Summary is available. Note that the case packet should also include documentation of the last relevant WHI hospitalization, if available. An autopsy report, if done, will be sufficient to complete this form if no Discharge Summary is available. If there is no Discharge Summary or autopsy report, only complete *Form 124* when a death certificate is available.

Form 125 – Summary of Hospitalization Diagnosis. Hospital discharge diagnosis. The FC will record the ICD-9-CM or ICD-10-CM diagnostic and procedure codes from the Face Sheet, Physician Attestation Sheet, or other coding abstract onto the form. The CCC Outcomes Liaison will review the forms for other possible outcomes.

Form 126 – Report of Thromboembolic Disease (HT). Diagnosis of PE or DVT for HT participants.

Form 130 – Report of Cancer Outcome. Diagnosis of cancer; completed by a CCC Cancer Coder.

Form 131 – Report of Hysterectomy (HT). Report of hysterectomy for HT participants only.

Form 132 – Report of Stroke Outcome. Diagnosis of a stroke (or TIA) and carotid artery disease; completed by stroke neurologist only.

8.6.5 Complete the Outcomes Reports

The *Investigation Documentation Summary* (*WHIX 0988*) is completed by the Physician Adjudicator after each case is adjudicated.

- Mark "Outcomes attached" if confirming that a WHI Extension Study outcome is present.
- Mark "no WHI Extension outcome" if **no** outcome is present. You **do not** need to complete any outcome form unless there is a WHI Extension Study defined hospital stay, in which case the Physician Adjudicator or CCC Outcomes Liaison needs to review the already completed *Form 125*.
- Mark "request for more documentation" to query for additional records because you have identified an additional potential outcome or need additional records to make an accurate diagnosis. To maintain consistency across FCs, request additional medical records (beyond the required documentation set) only if **essential** to make the diagnosis in a particular case.

8.6.6 OAC Review

The Physician Adjudicator has the option of requesting review of a case when feedback on the diagnosis is needed. To refer the case for Full Committee review:

- Make the best possible diagnosis
- Complete the *IDS* and any outcomes forms based on the available documentation.
- Mark "Full Committee Review" on the IDS if you have a procedural question or are not certain of the diagnosis. Include a detailed explanation of that request (i.e., what issue the OAC reviewers should address).

The questioned will be triaged and routed to an appropriate reviewer (senior Physician Adjudicator, CCC staff) or Full Committee. Feedback regarding the question will be provided. Based on the answer, the Physician Adjudicator updates/revises the diagnosis and completes the adjudication.

8.6.7 Return the Adjudication Cases to the CCC

Return only the original outcomes forms and attached IDS and packing sheet to the CCC, even if you determined there was no outcome for a case and you did not complete an outcomes form. Ensure that all forms and IDS reports for each case packet are complete and stapled or clipped together. Shred the participant medical records documentation upon adjudication completion. Return the forms and reports in the pre-paid return Fed-Ex slip included with each mailing.

8.6.8 Quality Assurance

Quality assurance of adjudication will be performed throughout the WHI Extension Study. A random sample of primary outcome cases will be re-adjudicated and both assigned diagnoses will be entered into the WHIX database. Secondly, for a given Committee, a selection of difficult cases will be sent to each Committee member to adjudicate. This is to ensure that all adjudicators apply the same criteria to confirm an outcome.

In addition, the CCC, the OAC, and PMC will monitor ascertainment and performance and make recommendations for performance enhancement and study-wide procedural changes.

8.7 Fatal Events Adjudication

8.7.1 Overview of Fatal Events

Mortality, as a clinical outcome, includes all-cause or total mortality and cause-specific mortality. Cause-specific mortality is classified as death due to cardiovascular diseases, cancer, injuries, or other causes. Fatal events in WHI Extension Study are classified as:

- **Total mortality**: The total number of deaths occurring in the WHI Extension Study for each of the respective studies and the components of each study (Hormone Therapy [HT], Dietary Modification [DM], Calcium and Vitamin D [CaD], Observational [OS]).
- **Cause-specific mortality**: Subclassified into:
  - Cancer, the 5 primary WHI cancers breast, endometrial, ovarian, colon, rectal cancer; lung and "other" cancers
  - Cardiovascular disease (CVD)
  - Injury
  - Other cause of death, which includes those conditions not listed above, e.g., non-cardiovascular, non-cancer, and non-traumatic death. A few of the more common "other" causes of death are listed with check boxes on the form in item 3; causes of death not listed should be coded "Other cause of death, known," and the underlying cause written in the blank of Qx. 2.1.
  - When the underlying cause of death cannot be determined from the information currently available, the case should be classified as "Unknown cause of death".

It is the Physician Adjudicator's responsibility to assign the final cause of death. This final decision may at times disagree with the causes of death identified on the death certificate. However, the decision should be based on a full review of the documents in the adjudication case packet. Occasionally the Physician Adjudicator may ask the CCC to have the FC obtain required documents that are missing.

8.7.2 Completing Additional Outcomes Forms

In addition to the cause(s) of death (as described below), the Physician Adjudicator should review the case packet for any other possible outcomes and either adjudicate those outcomes or forward to another committee to review (e.g., the stroke committee).

Cancer Deaths: If the cancer mentioned in the death certificate was not previously adjudicated, and was diagnosed after enrollment/randomization, indicate an additional committee review is required on the IDS and the case will be routed to the CCC Cancer Coders.

Cardiovascular Deaths: In the case of a hospitalized cardiovascular death/outcome, complete a *Form 121 – Report of Cardiovascular Outcomes*, if not already reported.

Deep Vein Thrombosis (DVT)/PE: For participants in the HT trial only, complete *Form 126 – Report of Venous Thromboembolic Disease (HT)* for all hospitalized DVT/PE. Complete *Form 126* if outpatient records confirm DVT or an autopsy report confirms PE.

8.7.3 Form 124 – Report of Death (Final)

The CCC Outcomes staff place the participant's barcode ID label in the space provided at the top of the form and route the appropriate outcome form and a copy of the supporting documents to the Physician Adjudicator for signature.

Administrative Questions:

Date Completed: Date the Physician Adjudicator completed the form.

Adjudicator Code: 5-digit ID for the Physician Adjudicator.

Central Case No.: Case number assigned by WHIX.

Case Copy No.: Copy number assigned by WHIX.

Qx.1 – Date of Death

Date of death is a required field and must be completed. Obtain the date of death from the Death Certificate. If a Death Certificate is not available, then use the medical records death summary, hospital records, *Form 120 – Initial Notification of Death*, or other sources, in that order.

Qx. 2 – Cause of Death

If death certificate diagnosis does not agree with available medical record information, then rely upon the medical records information which should generally be more detailed and accurate.

Occasionally, the Death Certificate is the only available document. In this case, code the underlying cause as mentioned on the Death Certificate. If the cause of death is incorrectly ordered on the death certificate, the Physician Adjudicator may code *Form 124 – Report of Death (Final)* according to what he/she thinks should be the sequence of events leading to death. In instances where this is the only documentation available it should be considered the most accurate determination of the cause of death. Use this information to code the underlying cause of death rather than marking "Unknown" cause of death.

At times, the Physician Adjudicator may need to return the adjudication case packet back to the CCC to follow-up with the FC OC to further investigate specific required documents that are missing.

Qx. 2.1 – Underlying cause: The disease or injury that initiated the events resulting in death.

The underlying cause of death is that one disease or condition believed to be mainly responsible for causing the woman's death. State the precise diagnosis in words. The study will use the underlying cause of death as the main classification for the death outcome. This field should never be left blank. If the underlying cause of death is unknown, enter "Unknown".

Qx. 2.2 – ICD-9-CM/ICD-10: Code corresponding to the underlying cause of death as listed on the Death Certificate or hospital face sheet, if available in the documentation. If not available, leave blank.

If the underlying cause of death is an accident/injury and the corresponding ICD-9-E-code or ICD-10-E-code is available, record the E-code in Qx. 3 – Subclassification of underlying cause of death, Accident/Injury. For example,

E⌊9⌋8⌋9⌋.⌊0⌋0⌋

Qx. 2.3 – CCC Use Only: Used to differentiate an ICD-9-CM from an ICD-10-CM code in WHIX.

Qx. 2.4, 2.7, and 2.10 – Contributory Cause(s) of Death: Indicate the events that contributed to the death but did not directly cause the death. Contributory cause(s) of death is/are the medical condition(s) that might have contributed to a death. For example, diabetes (contributory cause of death) in a patient with acute myocardial infarction (underlying cause). You may list between zero and three contributory causes of death. Hierarchic order not required.

Qx. 2.5, 2.8, and 2.11 – ICD-9-CM/ICD-10: The code corresponding to the contributory causes of death, if available.

If the immediate cause of death is the result of an accident/injury and the corresponding ICD-9-E-code or ICD-10-E-code is available, record the E-code in Qx. 3 – Subclassification of underlying cause of death, Accident/Injury. For example,

E└9┴8┴9┘.└0┴0┘

Qx. 2.6, 2.9, and 2.12 – CCC Use Only: Used to differentiate an ICD-9-CM from an ICD-10 in WHIX.

Qx. 2.13 – Immediate Cause: Final disease or condition resulting in death.

This is the terminal event. State the precise diagnosis in words. While cardiopulmonary arrest is present in all deaths, this is only an acceptable "immediate cause" in rare cases, e.g., when witnessed as sudden collapse with ventricular fibrillation or asystole. If an organ system failure, such as congestive heart failure, renal failure, hepatic failure, or respiratory failure is listed, that should be coded under immediate cause of death. Always report an etiology for the end stage condition as the underlying cause. For example, congestive heart failure (immediate cause of death) due to ischemic heart disease (underlying cause of death). This field may contain the same diagnosis as 2.1 – Underlying cause, or may be left blank.

Qx. 2.14 – ICD-9-CM/ICD-10: Code corresponding to the immediate cause of death, if available.

If the immediate cause of death is the result of an accident/injury and the corresponding ICD-9-E-code or ICD-10-E-code is available, record the E-code in Qx. 3 – Subclassification of underlying cause of death, Accident/Injury. For example,

E└9┴8┴9┘.└0┴0┘

Qx. 2.15 – CCC Use Only. Used to differentiate an ICD-9-CM from an ICD-10-CM code in WHIX.

Qx. 3 – Subclassification of Underlying Cause of Death (Required):

Select one and only one category to sub-classify underlying cause of death. Subclassification of the underlying cause of death in this question should reflect the "underlying cause of death" noted in **Qx. 2.1 – Subclassification of death**. This classification must be completed; it should never be left blank. If the cause of death is unknown, check box 99, "Unknown cause of death". The causes are grouped into the following four categories:

Cancer (codes 1-10) breast, ovarian, endometrial, colon, rectosigmoid junction, rectum, uterus, lung, other site, and unknown site.

Tips for Cancer Deaths

- If the cause of death is a metastatic cancer, and the primary site is known, then code the primary site as the cause of death and subclassification of the underlying cause under Qx. 3 should also be based on the primary site of cancer.
- When death certificate states colorectal cancer, review all available records to determine if primary site was colon or rectum.

- If the death certificate is the only available document, states colorectal primary, AND there is a history of either colon or rectal cancer, assume the colorectal cancer previously documented was the primary site at death. In this case, code the cancer site according to the previously adjudicated primary site of cancer, i.e., either colon or rectal.
- Case with Death Certificate only (no other information): If death certificate stating "colorectal" cancer is the only available document and there is no history of either colon or rectal cancer, then code this question as "4 – Colon". Also check the box on the IDS report to request review by the CA Committee and indicate what documentation in the present record suggests a cancer diagnosis. The CCC cancer coders will follow-up with this case to determine the primary site.
- Cancer of Sigmoid Colon: Sigmoid Colon is part of the colon and coded as colon cancer.
- Cancer of Appendix: Though the appendix is a part of the colon, WHI Extension Study does not include appendix in the primary colon cancer endpoint. Instead, code appendix to "8 – Other cancer" in this question and on *Form 130 – Report of Cancer* Outcome, Qx. 2-Primary site, code to "86 – Appendix".
- Cancer of Uterine Cervix is not included in Cancer of the Uterus. Code cancer of cervix as "8 – Other cancer" under subclassification of underlying cause of death.
- Chronic Leukemia/Lymphoma: These are considered a malignancy. If one is specified as the underlying cause of death (in Qx. 2.1), then code Qx. 3 to "8 – Other cancer".
- Myelo-proliferative disorders (Polycythemia vera, essential thrombocythemia): These are not considered malignancies and should be coded as "88 – Another cause of death, known".
- If a death certificate or medical records indicates "Uterine cancer", check prior adjudication documentation to determine if "endometrial cancer" was the correct pathologic diagnosis and code as endometrial, if appropriate. In the case without documented pathologic confirmation of endometrial or uterine (e.g., leiomyosarcoma of the uterus), code according to the terms used in the death certificate or in the available medical records.

Cardiovascular disease (codes 11-14, 18-19)

Tips for Cardiovascular Disease

- Definite Coronary Heart Disease (CHD) (code 11)

  No known non-CHD cause and at least one of the following: 1) documentation of chest pain within 72 hours of death and/or 2) history of chronic ischemic heart disease in the absence of valvular heart disease or non-CHD, and death certificate consistent with CHD as the underlying cause.

  Code definite CHD when the death certificate is consistent with death due to coronary disease and there is a history of chest pain before death or evidence of pre-existing coronary disease such as:

  - A history of CHD in the absence of valvular heart disease or non-CHD. History of CHD may be documented with a noted history of prior myocardial infarction, prior findings on catheterization or noninvasive testing, and prior coronary revascularization procedures in addition to confirmed prior WHI CHD as listed in hospital records or with confirmed prior outcomes listed on the accompanying Member Outcomes Status Report.
  - Use of nitroglycerin
  - Echocardiogram showing focal wall motion abnormalities.

  If Definite CHD is marked, also complete **Qx. 6 – Coronary Death** on the last page.

- Possible CHD (code 14)

  No known non-CHD cause, and death certificate is consistent with CHD as the underlying cause.

  Code possible CHD when the death certificate is consistent with death due to coronary disease, but there is no prior evidence of pre-existing coronary disease. Generally, an out-of-hospital sudden death is coded as possible CHD death if there is no other information available and in the absence of other possible causes.

  If Possible CHD is marked, also complete **Qx. 6 – Coronary Death** on the last page.

- Cerebrovascular disease (code 12)

  Includes ischemic and hemorrhagic strokes and excludes all subdural and epidural hematomas.

- Pulmonary embolism (code 13)

  Pulmonary embolism may be coded as the underlying cause of death if this diagnosis is supported by available hospital records, or in the absence of hospital records, if listed on the Death Certificate as the Cause of Death.

- Other cardiovascular disease (code 18)

  Use this code to encompass non-ischemic cardiomyopathy, alcoholic heart disease, myocarditis, valvular heart disease, congenital heart diseases, CHF (unrelated to coronary disease), aortic dissection, ruptured aortic aneurysm, and other cardiovascular causes.

- Unknown cardiovascular disease (code 19) – Use this code when inadequate information is available to allow determination of the kind of cardiovascular disease present, for example, if only a death certificate is available and it lists "cardiovascular disease" as the cause of death.

Accident/Injury (codes 21-23, 28)

- Homicide (code 21)
- Accident (code 22)
- Suicide (code 23)
- Other injury (code 28) – e.g., Undetermined if injury was accidentally or purposely inflicted.

"Other" Cause of Death (codes 31-36, 88, 99)

- Alzheimer's Disease (code 31) – Code if medical records or death certificate specifies the diagnosis as Alzheimer's Dementia. Code "Another cause of death, Known (88) medical records or death certificate states "Dementia" as the underlying cause of death.
- COPD (code 32)
- Pneumonia (code 33)
- Pulmonary Fibrosis (code 34)
- Renal Failure (code 35)
- Sepsis (code 36)
- Another cause of death, known (code 88)
- Unknown cause of death (code 99)

Tips for Other Cause of Death

- Other cause of death includes those conditions not listed above, e.g., non-cardiovascular, non-cancer, and non-traumatic death. A few of the more common "other" causes of death are listed with check boxes on the form in item 3. Code causes of death not listed on the form as "Other cause of death, known" and write the underlying cause in Qx. 2.1 – Underlying cause.

- When the underlying cause of death cannot be determined from the information currently available, the case should be classified as "Unknown cause of death".

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Qx. 4 – Was an Autopsy Performed?

This information is often documented on the Death Certificate. If death certificate is not available, record from *Form 120 – Initial Notification of Death*, if documented.

Qx. 5 – Documentation used for death adjudication

- Medical records documentation (current case only)
- Report of autopsy findings
- Death certificate
- ER record
- EMS report
- Informant interview
- *Form 120 – Initial Notification of Death*
- NDI Search (CCC searches only. Excludes Social Security Death Index [SSDI] FC searches.)
- Coroner's report
- Other, specify (e.g., a previously adjudicated case)

Mark all the documents used to complete *Form 124 – Report of Death (Fina*l). If a prior adjudication is used or any other document is reviewed but not listed, mark "Other" (code 8) and record the adjudication number and/or document(s) in the space provided.

Qx. 6 – Coronary Death (In and out-of-hospital deaths)

Complete for all deaths coded as definite CHD or possible CHD under Qx. 3 – Subclassification. For all in-hospital deaths, also complete *Form 121 – Report of Cardiovascular Outcome*.

Qx. 6.1 – Coronary Death Based On (Mark all that apply.)

- Hospitalized myocardial infarction within 28 days of death (code 1)
  A diagnosis of fatal MI must meet both the first and second criteria, a) and b) below, or the third criterion alone, c):
  a) No known non-atherosclerotic process or event
  b) And MI within 4 weeks prior to death (use criteria in *Section 8.8.2.1 – Myocardial Infarction*).
  c) Or autopsy evidence of acute MI.
- Previous angina, MI, or revascularization procedure is documented in the medical records, on the death certificate or by prior WHI adjudication and no known potentially-lethal non-coronary disease process (code 2)
- Coronary heart disease (CHD) diagnosed as cause of death at post-mortem examination (code 3)
- Death resulting from a CHD-related procedure, such as coronary bypass grafting (CABG) or percutaneous transluminal coronary angioplasty (PTCA) [For any death resulting from a revascularization procedure or an in-hospital death, complete *Form 121 – Report of Cardiovascular Outcome*] (code 4)
- Other (none of the above) (code 8)

Qx. 6.2 – Coronary Death Subclassification (Mark one.)

Mark the one category that applies best.

- Definite fatal MI (code 1): No known non-atherosclerotic cause (and death within 28 days of definite MI) or autopsy evidence of acute MI.
- Definite fatal CHD (code 2): No known non-atherosclerotic cause and at least one of the following:
  1) chest pain within 72 hours of death, or
  2) history of chronic ischemic heart disease in the absence of valvular heart disease or non-ischemic cardiomyopathy

- Possible fatal CHD (code 3): No known non-atherosclerotic cause, and death certificate consistent with CHD as the underlying cause.

Qx. 6.3 – Timing of Coronary Death (Mark one.)

Sudden Death (code 1) requires the presence of both characteristics listed below:

- Death witnessed as occurring within one hour after the onset of severe cardiac symptoms or within one hour after the participant was last seen without symptoms or during sleep,

  and

- Death occurs in the absence of potentially lethal non-coronary disease process

Rapid Death (code 2)

- Death occurs within 1-24 hours of symptom onset.

Other Coronary Death (code 3)

- Check if criteria are not fulfilled for sudden or rapid coronary death, or information regarding timing of coronary death is not available.

Figure 8.3
Form 124 – Report of Death (Final)

WHI **Form 124 - Report of Death (Final)** **Ver. 8.1**

OMB #0925-0414 Exp: 5/09

COMMENTS	- Affix label here- Member ID: __ __ __ __ - __ __ __ __ - __
To be completed by Physician Adjudicator Date Completed: __-__-__ (M/D/Y) Adjudicator Code: __-__	Central Case No.: __ __ __ __ __ __ __ Case Copy No.: __ __

1. Date of death: __-__-__ (M/D/Y)

2. Cause of death:

		ICD-9-CM/ICD-10-CM Codes	CCC use only
2.1.	**Underlying cause:** (Disease or injury that initiated events resulting in death.)	2.2. __ __ __.__ __	2.3. __ __
	Contributory cause(s) of death. (Contributory causes do not have to be listed in the hierarchical order.)		
2.4.		2.5. __ __ __.__ __	2.6. __ __
2.7.		2.8. __ __ __.__ __	2.9. __ __
2.10.		2.11. __ __ __.__ __	2.12. __ __
2.13.	**Immediate cause:** (Final disease or condition resulting in death.)	2.14. __ __ __.__ __	2.15. __ __

RV_____K_____V_____

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WHI **Form 124 - Report of Death (Final)** **Ver. 8.1**

3. Subclassification of underlying cause of death:
(Select only one underlying cause from the following 4 categories (Cancer, CVD, Accident, Other). One category must be completed.)

Cancer

- ☐ 1 Breast
- ☐ 2 Ovarian
- ☐ 3 Endometrial
- ☐ 4 Colon
- ☐ 5 Rectosigmoid junction
- ☐ 6 Rectum
- ☐ 7 Uterus
- ☐ 10 Lung
- ☐ 8 Other Cancer _____
- ☐ 9 Unknown cancer site

Cardiovascular disease

- ☐ 11 Definite Coronary Heart Disease (CHD)
  (No known non-CHD cause and at least one of the following: (1)-chest pain within 72 hours of death and/or (2)-history of chronic ischemic heart disease in the absence of valvular heart disease or non-CHD, and death certificate consistent with CHD as the underlying cause.)
- ☐ 14 Possible Coronary Heart Disease (CHD)
  (No known non-CHD cause, and death certificate consistent with CHD as the underlying cause.)

→ **If box 11 or 14 marked, complete Question 6 on the next page.**

- ☐ 12 Cerebrovascular disease
- ☐ 13 Pulmonary Embolism
- ☐ 18 Other cardiovascular disease
- ☐ 19 Unknown cardiovascular disease

Accident/Injury

- ☐ 21 Homicide
- ☐ 22 Accident
- ☐ 23 Suicide
- ☐ 28 Other injury

"Other" Cause of Death

- ☐ 31 Alzheimer's Disease
- ☐ 32 COPD
- ☐ 33 Pneumonia
- ☐ 34 Pulmonary Fibrosis
- ☐ 35 Renal Failure
- ☐ 36 Sepsis
- ☐ 88 Another cause of death, known
- ☐ 99 Unknown cause of death

WHI **Form 124 - Report of Death (Final)** **Ver. 8.1**

4. Was an autopsy performed? **(*Mark one.*)**
   - ☐ 0 No
   - ☐ 1 Yes
   - ☐ 9 Unknown

5. Documentation used for death adjudication **(Mark all that apply)**:
   - ☐ 1 Medical records documentation (current case only)
   - ☐ 2 Report of autopsy findings
   - ☐ 3 Death certificate
   - ☐ 4 ER record
   - ☐ 5 EMS report
   - ☐ 6 Informant interview
   - ☐ 7 *Form 120 – Initial Notification of Death*
   - ☐ 9 **NDI Search (CCC use only)**
   - ☐ 10 Coroner's report
   - ☐ 8 Other _____ (e.g., a previously adjudicated case)

6. Coronary Death ***(In and out of hospital deaths)***

   6.1. **Coronary death based on:** ***(Mark all that apply.)***
   - ☐ 1 Hospitalized myocardial infarction within 28 days of death
   - ☐ 2 Previous angina, myocardial infarction, or revascularization procedure and no known potentially-lethal non-coronary disease process
   - ☐ 3 Coronary heart disease (CHD) diagnosed as cause of death at post-mortem examination
   - ☐ 4 Death resulting from a CHD-related procedure, such as coronary bypass grafting (CABG) or percutaneous transluminal coronary angioplasty (PTCA) **[For any death resulting from a revascularization procedure or an in hospital death, complete *Form 121 – Report of Cardiovascular Outcome*]**
   - ☐ 8 Other (none of the above)

   6.2. **Coronary death subclassification:** ***(Mark the one category that applies best.)***
   - ☐ 1 Definite fatal MI: no known non-atherosclerotic cause (and death within 28 days of definite MI) or autopsy evidence of acute MI
   - ☐ 2 Definite fatal CHD: no known non-atherosclerotic cause and at least one of the following: (1) chest pain within 72 hours of death, or (2) history of chronic ischemic heart disease in the absence of valvular heart disease or non-ischemic cardiomyopathy
   - ☐ 3 Possible fatal CHD: no known non-atherosclerotic cause, and death certificate consistent with CHD as the underlying cause

   6.3. **Timing of coronary death: (Mark one.)**
   - ☐ 1 Sudden death: death occurring within one hour of symptom onset or after the participant was last seen without symptoms, and death occurs in the absence of potentially lethal non-coronary disease process
   - ☐ 2 Rapid death: death occurs within 1-24 hours of symptom onset
   - ☐ 3 Other coronary death (Does not fulfill criteria for sudden or rapid coronary death.)

_____
Responsible Adjudicator Signature

NOTE: If this is a hospitalized death, or an autopsy report is available, adjudicate any WHI outcomes using the appropriate outcomes form.

8.8 Cardiovascular Outcomes

Specific CVDs are primary or secondary outcomes for the WHI Extension Study. The diagnosis of cardiovascular events is derived from a constellation of signs, symptoms, and objective evidence such as serum enzyme levels, diagnostic tests and procedure reports. These constellations for diagnosis may be different for different patients and the systematic assignment of cardiovascular outcomes diagnoses will be a challenge to the Physician Adjudicators.

This section describes the study-defined diagnostic criteria for the cardiovascular outcomes and outlines the necessary documentation to arrive at consistent diagnoses. Note that thromboembolic outcomes (i.e., deep vein thrombosis and pulmonary embolus are described in detail in *Section 8.9 – Other Outcomes*).

For WHI Extension Study purposes, CHD includes MI, coronary death, and coronary revascularization. The possible diagnoses of CHD will be based on:

- A reported hospitalization with appropriate documentation for CHD.
- A report of a death possibly due to heart disease with appropriate documentation.

The processing of CVD outcomes follows the established procedures for ascertainment and adjudication of outcomes as outlined in *Figure 8.1 – Ascertainment and Adjudication Process*. Refer to *Sections 8.2 – 8.6* for more details on this multi-step, multi-component process.

Each cardiovascular adjudication "case packet" includes a blank *Form 121 – Report of Cardiovascular Outcome* and other outcomes forms as needed, to be completed. There may be more than one suspected cardiovascular outcome in the case packet. If there are multiple CVD outcomes in one hospitalization, the Physician Adjudicator should record them all on one *Form 121 – Report of Cardiovascular Outcome*. There may also be CVD outcomes in case packets created for a hospitalization in which the participant did not self-report a CVD outcome. Thus, the Physician Adjudicator should keep a supply of *Form 121*s on hand.

8.8.1 Diagnostic Categories

The following cardiovascular diagnoses are monitored during the WHI Extension Study. (Thromboembolic diagnoses are discussed in *Section 8.9 – Other Outcomes*.)

Obtained through self-report only:

- Angina pectoris (self-report on *Form 33*).
- Congestive heart failure (nonfatal) (self-report on *Form 33*).

Adjudicated outcome using *Form 121 – Report of Cardiovascular Outcome:*

- Myocardial infarction (MI) (definite, probable, or aborted). (See *Table I, Form 121*.)
- Coronary death.
- Coronary revascularization (CABG and PTCA).
- Carotid artery disease requiring hospitalization (also on *Form 132*)
- Peripheral arterial disease requiring hospitalization.
- TIA that results in a hospitalization of 2 nights or more is adjudicated for a possible stroke.
- Angina and CHF that result in a hospitalization of 2 nights or more are adjudicated for a possible myocardial infarction.

Adjudicated outcome using *Form 132 – Report of Stroke Outcome:*

- Stroke (fatal and nonfatal, hemorrhagic, ischemic, or unknown); includes inpatient and outpatient strokes.
- Transient ischemic attack (TIA)
  - self-report on *Form 33*
- Any denied stroke determined to be a TIA is recorded using *Form 132 – Report of Stroke Outcome*
- Carotid artery disease requiring hospitalization (also on *Form 121*).

Adjudicated outcome using *Form 124 – Report of Death (Final)* (see *Section 8.7 – Fatal Events*)

- Definite coronary heart disease (CHD) death
- Possible CHD death
- Other cardiovascular disease
- Unknown cardiovascular disease

Adjudicated outcome using *Form 125 – Summary of Hospitalization Diagnosis:*

- Other cardiovascular event associated with hospitalization of 2 nights or more and selected hospital stays of one or more nights.

8.8.2 Other Cardiovascular Events Associated with a Hospital Stay of 2 Nights or More

Any other cardiovascular event not fitting the above categories, yet requiring a hospital stay of 2 nights or more, are classified as "other cardiovascular events." Information on these events is collected from the hospital face sheet and/or Physician Attestation Sheet and recorded on *Form 125 – Summary of Hospitalization Diagnosis*. Do not complete *Form 121 – Report of Cardiovascular Outcome* for these outcomes. These other cardiovascular events include but are not limited to the following:

- Thoracic aortic aneurysm
- Valvular heart disease
  - aortic valve stenosis
  - aortic valve regurgitation
  - mitral valve stenosis
  - mitral valve regurgitation
  - mitral valve prolapse
- Endocarditis
- Pericarditis
- Cardiac tamponade
- Cardiac hypertrophy
- Cardiomyopathy
- Upper extremity peripheral vascular disease
- Aortic dissection

8.8.3 First vs. Subsequent Cardiovascular Disease

See *Section 8.3.2 – First vs. Recurrent Events* and *Table 8.3 – Subsequent Conditions* for a description of which subsequent cardiovascular outcomes are adjudicated. Document a first MI **and**, as appropriate, a second MI (one occurring during or as a result of a procedure during the same hospital stay) on *Form 121 – Report of Cardiovascular Outcome*. A subsequent myocardial infarction or stroke occurring during the WHI Extension Study does not require investigation unless the subsequent report is part of a hospital stay of 2 nights or more. In this case, the CCC Outcome Liaisons will typically adjudicate these hospital stays. Note that if the participant had an MI or stroke before WHI randomization or enrollment, her **first** MI or stroke after WHI enrollment would be counted as her first MI for study purposes.

8.8.4 Documentation Requirements

Table 8.2 – Required Documents for Outcomes indicates the various medical record documents required and recommended for each type of cardiovascular outcome. The essential documents are indicated with an **×** in a box (☒) and the recommended documents are indicated with an **×**.

Physician adjudicators are strongly encouraged to rely on the documentation requirements approved by the Outcomes Adjudication Committee, as listed in *Table 8.2 – Required Documents for Outcomes*. Use of these documents ensures standardized document sets among Field Centers.

8.8.5 Form 121 – Report of Cardiovascular Outcomes

A Physician Adjudicator completes *Form 121 – Report of Cardiovascular Outcomes* when a participant reports having had one or more of the WHI Extension Study cardiovascular outcomes listed below:

- Definite or probable myocardial infarction. (*Note:* Angina and CHF that result in a hospital stay of 2 nights or more are adjudicated for a possible MI. Neither is specifically recorded on *Form 121*.)
- Coronary death
- Coronary revascularization (including outpatient coronary revascularization)
- Carotid artery disease requiring hospitalization
- Peripheral arterial disease requiring hospitalization

Administrative Questions

Date Completed: Date the Physician Adjudicator completed the form.

Adjudicator Code: 5-digit ID for the Physician Adjudicator.

Central Case No.: Case number assigned by WHIX.

Case Copy No.: Copy number assigned by WHIX.

Qx. 1 – ECG Pattern

Complete for a confirmed MI, coronary death (hospitalized), and coronary revascularization. Read all ECGs in the case packet. Carefully note the date of each ECG to verify that it pertains to the dates of the event being adjudicated.

Mark the one category that best describes the serial evolution of ECG pattern based on all available ECGs. If there is only one ECG, by definition you will not be able to evaluate evolving ECG patterns.

- Evolving Q-wave and evolving ST-T abnormalities (code 1)
  - Requires serial ECGs.
  - Will usually reflect clinical ST elevation MI (STEMI) with Q waves.
- Equivocal Q-wave evolution; or evolving ST-T abnormalities; or new left bundle branch block (code 2).
  - Requires serial ECGs demonstrating typical deep, symmetric T wave inversion and evolution over hours to days. Will not appear as downsloping ST-T changes associated with LVH. Changes must evolve over time.
  - Mark if there is documentation in the medical record indicating the left bundle branch block (LBBB) is new. Otherwise, mark 'Code 8 - Other ECG pattern, ECG uncodable, or normal ECG pattern.'
- Q-waves or ST-T abnormalities suggestive of an MI and not classified as code 1 or 2 above (code 3).
- Do not code if Q-wave is old, by documentation in medical record, the ECG interpretation or by serial ECG showing no typical evolution of acute MI.
- Other ECG pattern, ECG uncodable, or normal ECG pattern (code 8)
  - For left bundle branch block, mark if documentation in the medical record indicates that the pattern is old. Mark this code if LBBB is documented in the medical record, but ECG is not available.
- ECG not available (code 9)

Recommended Readings for ECG Interpretation

Crow, R.S., Prineas, R.J., Jacobs, D.R., et al. (1989). A new epidemiologic classification system for Interim Myocardial Infarction for Serial Electrocardiographic Changes. *American Journal of Cardiology*, 64:454-461.

Dubin, D. (1996). *Rapid interpretation of EKG's*, 5th edition. Tampa, Florida; Cover Publishing Co.

Goldschlager, N., and Goldman, M.J. (1989). *Principles of Clinical Electrocardiography*, 3rd edition. Norwalk, CT; Appleton Lange.

Qx. 2 – Cardiac enzyme information available

Complete for a confirmed MI, coronary death (hospitalized), and coronary revascularization.

Pertinent enzyme results (as defined in the following Qx 2 subquestions below) include those recorded in the hospital chart for days 1 through 4 after hospital admission, or days 1 through 4 after an in-hospital CHD event. Information on any non-ischemic causes for elevated enzymes is on the hospital discharge summary. Code the enzymes for the timing of the symptoms evaluation.

Cardiac Enzymes

If the actual laboratory report is not available in the case packet, the enzyme results, in some instances can still be recorded on *Form 121*.

- If enzymes are stated to be "normal" they can be recorded as such.
- If described as "abnormal" or a specific value is given, code only as >2 x ULN if this is unquestionably true.
- If enzymes stated to be abnormal without quantification, mark enzymes as "not available".

A summary of the enzyme diagnostic criteria is given in *Table 8.8 – Cardiac Enzyme Diagnostic Criteria* and define the cardiac enzyme interpretations listed in *Table 8.7 – Diagnosis of Myocardial Infarction*.

Qx. 2.1 – Creatine Kinase Heart Fraction (CK-MB)

CK-MB is expressed as a percent, index, or unit. WHI criteria for abnormal level require CK-MB value to be greater than or equal to twice the upper limit of normal for that hospital lab (if upper limit is given in the lab report) then it is classified as elevated. For options referring to "normal limits," use the limits specified by the laboratory that conducted the test.

Note that the total CK may be elevated for reasons other than myocardial infarction and there may also be non-ischemic causes for the elevated CK-MB, such as cardiac surgery, cardiac defibrillation, severe muscle trauma, or rhabdomyolysis.

If CK-MB is available

- **expressed as a % or index**: (Record peak results only.)
  - CK-MB at least 2x upper limit of normal for % or index (code 1)
  - CK-MB greater than upper limit of normal but less than 2x upper limit of normal for % or index (code 2)
  - CK-MB within normal limits for % or index (code 3)
- **expressed in units** (usually ng/ml): (Record peak results only.)
  - CK-MB at least 2x upper limit of normal for units (code 4)
  - CK-MB greater than upper limit of normal but less than 2x upper limit of normal for units (code 5)
  - CK-MB within normal limits for units (code 6)

If CK-MB not available

- Total CK at least 2x upper limit of normal (code 9)
- Total CK greater than upper limit of normal but less than 2x upper limit of normal (code 10)
- Total CK within normal limits (code 11)

CK result not available (code 99)

- Check if CK was not measured or if no result is available

Qx. 2.2 – Troponin Lab Test

Mark the one category that applies best. If more than one Troponin test was conducted, indicate the type that was most elevated.

- Troponin C (code 1)
- Troponin I (code 2)
- Troponin T (code 3)
- Troponin not specified (code 4)
- Troponin not available (code 9)

If Troponin was not measured or if no result is available, mark "Troponin not available" and skip to Qx. 3 – Cardiac-Pain.

Qx. 2.2.1 – Results (Troponin)

Mark the one category that applies best. Code Troponin values using the upper limit of normal (ULN) and not upper limit of indeterminate/indecisive as the reference value. For example, if two cut points are given, choose the lower cut point for the upper limit of normal.

If more than one Troponin test was conducted, record the levels for the type that was most elevated. For the option referring to "normal limits," use the limit specified by the laboratory that conducted the test.

- Troponin at least 2x upper limit of normal (code 1)
- Troponin greater than upper limit of normal but less than 2x upper limit of normal (code 2)
- Troponin within normal limits (code 3)
- Other (code 9)

Qx. 3 – Cardiac Pain

Complete for a confirmed MI, coronary death, and coronary revascularization.

Cardiac pain refers to an acute episode of pain, discomfort, or tightness in the chest, arm, throat, or jaw, as defined below:

- Chest, jaw, throat, or arm pain, discomfort, or tightness of at least 15 minutes duration probably due to myocardial ischemia.
- Other equivalent ischemic symptoms, e.g., abrupt onset of shortness of breath, nausea, back pain, weakness, etc., if the medical records reasonably supports that these symptoms are produced by the myocardial infarction.
- And an absence of a definite non-cardiac cause of chest pain.

Qx. 4 – Myocardial Infarction: definite, probable, or aborted MI

Myocardial infarction is defined as the death of part of the myocardium due to an occlusion of a coronary artery from any cause, including spasm, embolus, thrombus, or the rupture of a plaque.

Use the responses to Qx. 1 – 3 about ECG, cardiac enzymes, and cardiac pain to determine the occurrence of a myocardial infarction (MI). See *Table 8.7 – Diagnosis of Myocardial Infarction*. Physician Adjudicators may use clinical judgment to assess the diagnosis of an MI if the criteria in *Table 8.7* do not fit the particular case.

Aborted Myocardial Infarction

A diagnosis of aborted MI must meet all of the following criteria:

- Symptoms and ECG evidence for acute MI at presentation.
- Intervention (e.g., thrombolytic therapy procedure) is followed by resolution of ECG changes.
- All cardiac enzymes measured after the intervention is within normal limits.

Qx. 4.1 – Date of Admission

The **admit date** on the hospital medical records or the date of diagnosis on the outpatient medical records (PTCA only).

Qx. 4.2 – Diagnosis

Mark the one category that corresponds to whether or not the MI occurred as a result of or during a procedure.

- MI not occurring as a result of or during a procedure (code 1)
- MI occurred during a procedure or resulting from a procedure within 30 days (code 2)

Qx. 4.2.1 – Type of Procedure

Mark the one category that apples best:

- A myocardial infarction that followed a cardiac procedure within 24 hours (for example, diagnostic coronary catheterization, percutaneous coronary intervention, CABG, pacemaker insertion, or cardioversion) (code 1)
- A myocardial infarction that followed a cardiac procedure within 2-30 days (for example, diagnostic coronary catheterization, percutaneous coronary intervention, CABG, pacemaker insertion, or cardioversion) (code 2)
- A myocardial infarction that followed a non-cardiac procedure within 30 days (for example, any elective or emergency non-cardiac vascular procedure regardless of type of anesthesia, or any elective or emergency surgical procedure requiring more than local anesthesia) (code 3)

Qx. 4.3 – Was thrombolytic agent administered or emergent revascularization procedures performed

An emergent revascularization is defined as occurring within 12 hours of symptom onset. Mark in this Qx. and in **Qx. 6 – Coronary revascularization**. Code non-emergent revascularization procedures only under Qx. 6. Examples of thrombolytic agents are streptokinase, reteplase (Retavase), tenecteplase (TNKase), alteplase tPA (Activase).

Table 8.7
Diagnosis of Myocardial Infarction

	Cardiac Enzyme Interpretation (see *Table 8.8* below)			
	Abnormal	**Equivocal**	**Incomplete**	**Normal**
ECG Pattern/Symptoms				
Cardiac pain present:				
Evolving Q wave and evolving ST-T abnormalities	Definite MI	Definite MI	Definite MI	Definite MI
Equivocal Q wave evolution; or evolving ST-T abnormalities, or new left bundle branch block	Definite MI	Definite MI	Probable MI	No MI
Q waves or ST-T abnormalities suggestive of an MI and not classified above	Definite MI	Probable MI	No MI	No MI
Other ECG, ECG absent or uncodable	Definite MI	No MI	No MI	No MI
Cardiac Pain absent:				
Evolving Q wave and evolving ST-T abnormalities	Definite MI	Definite MI	Definite MI	Probable MI
Equivocal Q wave evolution; or evolving ST-T abnormalities; or new left bundle branch block	Definite MI	Probable MI	No MI	No MI
Q waves or ST-T abnormalities suggestive of an MI and not classified above	Probable MI	No MI	No MI	No MI
Other ECG, ECG absent or uncodable	No MI	No MI	No MI	No MI

Table 8.8
Cardiac Enzyme Diagnostic Criteria

		Interpretation	
Cardiac Enzyme	**Abnormal***	**Equivocal**	**Normal**
Creatine kinase MB fraction (CK-MB)	≥ 2x ULN (as %, index, or units); or "present" without quantification	1-2x ULN (as %, index, or units); or "weakly present"	WNL
Toponin (C, I, or T)**	Troponin ≥ 2x ULN	Troponin 1-2x ULN	Troponin is WNL
Total creatine kinase (CK) (no MB available)	N/A	Total CK ≥ 2x ULN	Total CK is 1-2x ULN or WNL

ULN = upper limit of normal
WNL = within normal limits

* If both CK-MB and Troponin are available, Troponin must be elevated to be considered abnormal, if only CK-MB is available, abnormal levels are enough to code enzymes as abnormal, i.e., WHI considers Troponin as the most accurate indicator of myocardial injury.

** Code Troponin levels using the ULN and not Upper limit of undeterminate/indecisive as the reference value. Thus, if 2 cut points are given, choose the lower cut point for the ULN.

Qx. 4.4 – Was the MI fatal?

Mark one. If Yes, complete **Qx. 5 – Coronary death** (for hospitalized deaths) and *Form 124 – Report of Death (Final*).

Qx. 5 – Coronary Death (hospitalized deaths only)

Coronary death is defined as death consistent with coronary heart disease as the underlying cause **plus** any one of the following:

- Pre-terminal hospitalization with myocardial infarction within 28 days of death.
- Previous angina, myocardial infarction, or revascularization procedure, and no known potentially-lethal non-coronary disease process.
- Death resulting from a procedure related to coronary artery disease such as CABG or percutaneous coronary intervention.

Ascribe deaths due to a non-coronary underlying cause in which the terminal event was an MI to the underlying cause - not to CHD.

Coronary death is subclassified as:

- Definite fatal MI: no known non-atherosclerotic cause **and** definite MI within 4 weeks of death or autopsy evidence of acute MI.
- Definite fatal CHD: no known non-atherosclerotic cause **and** one or both of the following: chest pain within 72 hours of death or a history of chronic ischemic heart disease (in the absence of valvular heart disease or non-ischemic cardiomyopathy.)
- Possible fatal CHD: no known non-atherosclerotic cause **and** death certificate consistent with CHD as underlying cause.

A death certificate should be obtained if at all possible, for all deaths (see *Section 8.7 – Fatal Events* for detail on adjudicating fatal events).

- For in-hospital death, also review the hospital discharge summary/death summary and autopsy report (if available).
- For out of hospital death, review the coroner's or medical examiner's report and autopsy report (if available).

Qx. 5.1 – Date of Death

The date on the death certificate or the date of death listed on the hospital medical records.

Qx. 5.2 – Diagnosis

Record the type of coronary death in words, e.g., definite CHD death, possible CHD death, fatal MI, fatal CABG. (This data item is not data entered.)

Qx. 6 – Coronary Revascularization

Coronary revascularization includes surgery or other procedures that are intended to provide improved coronary blood flow to the myocardium. This would include:

- CABG
- Percutaneous Coronary Intervention:
  - Coronary stent
  - Balloon
  - Artherectomy
  - Laser

Note that **Qx. 1 – ECG** and **Qx. 2 – Cardiac Enzyme Information** must be completed, if available.

Qx. 6.1 – Date of admission

Use the date of admission as the date of procedure, even if more than one procedure was done. If the percutaneous coronary intervention was performed on an outpatient basis, record the date of the intervention.

Qx. 6.2 – Type of procedure

Mark all that apply. If multiple procedures of the same type (e.g., two PTCAs) were conducted during a single hospital admission, record only the first procedure. Complete two *Form 121*s if both a CABG and PTCA were conducted during the same hospital admission.

- CABG (code 1)
- PTCA, coronary stent, or coronary atherectomy (code 2)

Qx. 6.3 – Second MI

Mark one. Mark only if a second MI not already reported in *Qx. 4.2.2 – Definite, Probable, or Aborted MI* occurred at this admission as a result of or during the coronary revascularization procedure.

Mark 'No' if enzymes were drawn after the revascularization and there is no evidence for an MI.

Mark 'Yes' if enzymes were drawn after the revascularization and there was evidence for an MI.

Mark 'Unknown' if no enzymes were drawn after the procedure or enzyme results are not available.

Qx. 7 – Carotid Artery Disease Requiring and/or Occurring During Hospitalization

Disease must be symptomatic and/or requiring intervention (i.e., vascular or surgical procedure). Mark the appropriate box and complete Qx. 7.1 to 7.3 to confirm the carotid artery disease.

Qx. 7.1 – Date of admission

The admit date on the medical records.

Qx. 7.2 – Diagnosis

Mark the one box that corresponds best to the Physician Adjudicator's final diagnosis.

- Carotid artery occlusion and stenosis without documentation of cerebral infarction (code 1)
- Carotid artery occlusion and stenosis with documentation of cerebral infarction (code 2)

Qx. 7.3 – Carotid Artery Disease Based on:

Mark all that apply. Note that participant must be hospitalized plus have one or more of the following:

- Symptomatic disease with carotid artery disease listed on the hospital discharge summary (code 1)
- Symptomatic disease with abnormal findings (≥ 50% stenosis) on carotid angiogram, MRA, or Doppler flow study (code 2)
- Vascular or surgical procedure to improve flow to the ipsilateral brain (code 3)

Qx. 8 – Peripheral Arterial Disease Requiring and/or Occurring During Hospitalization

Peripheral arterial disease is defined as hospitalization for leg pain produced by ischemia from peripheral arterial disease; or hospitalization with a positive diagnostic test result or surgical intervention for lower extremity arterial occlusion or abdominal aortic aneurysm.

This diagnosis refers to diseases in the abdominal aorta, iliac arteries, or below that are symptomatic and/or require intervention; symptomatic disease includes intermittent claudication, ischemic ulcers, gangrene, or surgery for amputation; and requires or occurs during a hospitalization. It includes abdominal aortic aneurysm but excludes aortic dissection and thoracic aortic aneurysm.

The first report of peripheral arterial disease is investigated and adjudicated. Subsequent report of a *different* type of peripheral arterial disease should also be documented and classified.

Qx. 8.1 – Date of admission

The admit date on the medical records.

Qx. 8.2 – Diagnosis

Mark the one box that corresponds best to the Physician Adjudicator's final diagnosis. If the participant is diagnosed with two of the diagnoses listed, e.g., an arterial embolism and a AAA, complete 2 separate *Form 121*s.

- Lower extremity claudication (code 1)
- Atherosclerosis of arteries of the lower extremities (code 2)
- Arterial embolism and/or thrombosis of the lower extremities (code 3)
- Abdominal aortic aneurysm (AAA) (code 4)

Qx. 8.3 – Peripheral artery disease based on:

Defined by hospitalization plus one or more of the following: Mark all that apply.

- Ultrasonographically- or angiographically-demonstrated obstruction, or ulcerated plaque (≥ 50% of the diameter or ≥ 75% of the cross-sectional area) demonstrated on ultrasound or angiogram of the iliac arteries or below (code 1)
- Absence of pulse by Doppler in any major vessel of lower extremities (code 2)
- Exercise test that is positive for lower extremity claudication (code 3)
- Surgery, angioplasty, or thrombolysis for peripheral arterial disease (code 4)
- Amputation of one or more toes or part of the lower extremity because of ischemia or gangrene (code 5)
- Exertional leg pain relieved by rest and at least one of the following: (1) claudication diagnosed by physician, or (2) ankle-arm systolic blood pressure ratio ≤ 0.8 (code 6)
- Ultrasonographically- or angiographically-demonstrated abdominal aortic aneurysm (code 7)
- Surgical or vascular procedure for abdominal aortic aneurysm (code 8)

Responsible Adjudicator Signature

The Physician Adjudicator should sign the form only when s/he is satisfied that the questions on the cardiovascular outcomes being reported have been filled in as completely and accurately as possible on the basis of all available information, and that other outcomes (e.g., hospitalization) have been investigated and adjudicated.

Figure 8.4
Form 121 – Report of Cardiovascular Outcome

Form 121 - Report of Cardiovascular Outcome Ver. 8.1

OMB# 0925-0414 Exp: 5/09

COMMENTS	-Affix label here- Member ID: __ __ __ __ - __ __ __ __ - __
To be completed by Physician Adjudicator Date Completed: __-__-__ (M/D/Y) Adjudicator Code: __-__	Central Case No.: __ __ __ __ __ Case Copy No.: __

(For items 1-8, each question specifies "mark one" or "mark all" that apply.)

Complete Q1 - ECG, Q2 - cardiac enzyme, and Q3 - cardiac pain information for the following WHI Extension Study outcomes: Myocardial infarction (MI), coronary death [hospitalized], and coronary revascularization

1. ECG pattern: ***(Mark the one category that applies best.)***

- ☐ 1 Evolving Q-wave and evolving ST-T abnormalities
- ☐ 2 Equivocal Q-wave evolution; or evolving ST-T abnormalities; or new left bundle branch block
- ☐ 3 Q-waves or ST-T abnormalities suggestive of an MI and not classified as code 1 or 2 above
- ☐ 8 Other ECG pattern, ECG uncodable, or normal ECG pattern
- ☐ 9 ECG not available

2. Cardiac enzyme information available?

- ☐ 0 No ⟶ ***Skip to Question 3 on page 2.***
- ☐ 1 Yes

2.1. Serum creatine kinase (CK): ***(Mark all that apply.) (Always record % or index if available.)***

If CK-MB available:

CK-MB expressed as a % or index: (*Record peak results only.*)

- ☐ 1 CK-MB at least 2x upper limit of normal for % or index
- ☐ 2 CK-MB greater than upper limit of normal but less than 2x upper limit of normal for % or index
- ☐ 3 CK-MB within normal limits for % or index

CK-MB expressed in units (usually ng/ml): *(Record peak results only.)*

- ☐ 4 CK-MB at least 2x upper limit of normal for units
- ☐ 5 CK-MB greater than upper limit of normal but less than 2x upper limit of normal for units
- ☐ 6 CK-MB within normal limits for units

If CK-MB not available:

- ☐ 9 Total CK at least 2x upper limit of normal
- ☐ 10 Total CK greater than upper limit of normal but less than 2x upper limit of normal
- ☐ 11 Total CK within normal limits
- ☐ 99 CK result not available

WHI **Form 121 - Report of Cardiovascular Outcome** **Ver. 8.1**

2.2. Troponin lab test. ***(Mark the one category that applies best.)*** **(If more than one test was conducted, record the type with the most elevated lab result.)**

☐1 Troponin C
☐2 Troponin I
☐3 Troponin T
☐4 Troponin, not specified
☐9 Troponin not available ⟶ ***Skip to Question 3 below.***

2.2.1 Results ***(Mark the one category that applies best.)*** Troponin values should be coded using the upper limit of normal (ULN) and not upper limit of indeterminate/indecisive as the reference value. Thus, if 2 cutpoints are given, choose the lower cutpoint for the upper limit of normal.

☐1 Troponin at least 2x upper limit of normal
☐2 Troponin greater than upper limit of normal but less than 2x upper limit of normal
☐3 Troponin within normal limits
☐9 Other

3. Cardiac pain defined as: an acute episode of pain, discomfort or tightness in the chest, arm, throat or jaw: *(Mark the one category that applies best.)*

☐1 Present
☐2 Absent
☐9 Unknown/Not recorded

Yes **No**
☐1 ☐0 **4. Definite, probable, or aborted myocardial infarction (See excerpts from *Table 8.5.1 – Definition of Criteria for Diagnosis of Myocardial Infarction* and *Table 8.5.2 – Algorithm for Enzyme Diagnostic Criteria* on the last page of this form.)**

4.1. Date of admission: ___ - ___ - ___ (M/D/Y)

4.2. Diagnosis: ***(Mark one.)***

☐1 Myocardial infarction not occurring as a result of or during a procedure ⟶ ***Skip to Question 4.3 on the next page.***

☐2 Myocardial infarction during or resulting from a procedure, i.e., within 30 days of any procedure.

4.2.1. Type of Procedure ***(Mark one.)***

☐1 A myocardial infarction that followed a cardiac procedure within 24 hours (for example, diagnostic coronary catheterization, percutaneous coronary intervention, CABG, pacemaker insertion, or cardioversion).

☐2 A myocardial infarction that followed a cardiac procedure within 2-30 days (for example, diagnostic coronary catheterization, percutaneous coronary intervention, CABG, pacemaker insertion, or cardioversion).

☐3 A myocardial infarction that followed a non-cardiac procedure within 30 days (for example, any elective or emergency non-cardiac vascular procedure regardless of type of anesthesia, or any elective or emergency surgical procedure requiring more than local anesthesia).

WHI **Form 121 - Report of Cardiovascular Outcome** **Ver. 8.1**

4.3 Was a thrombolytic agent administered or emergent* revascularization procedure (e.g., angioplasty or stent) performed? ***(Mark one.)***

*An emergent revascularization is conducted within 12 hours of symptom onset; code both here and in Q6. Non-emergent revascularization procedures are coded only under Q6. Examples of thrombolytic agents are streptokinase, reteplase (Retavase), tenecteplase (TNKase), alteplase tPA (Activase).

☐ 0 No
☐ 1 Yes
☐ 9 Unknown

4.4. Was the myocardial infarction fatal? ***(Mark one.)***

☐ 0 No
☐ 1 Yes ***(Complete Question 5 below [for hospitalized deaths only] and Form 124 - Final Report of Death.)***

For <u>hospitalized</u> deaths only:

Yes ☐ 1 **No** ☐ 0 **5. Coronary death *(Complete Form 124 - Final Report of Death.)***

5.1. Date of Death: ⌊__⌋⌊__⌋ - ⌊__⌋⌊__⌋ - ⌊__⌋⌊__⌋ (M/D/Y)

5.2. Diagnosis:_____

Yes ☐ 1 **No** ☐ 0 **6. Coronary revascularization**

6.1. Date of Admission/Procedure: ⌊__⌋⌊__⌋ - ⌊__⌋⌊__⌋ - ⌊__⌋⌊__⌋ (M/D/Y)

6.2. **Type of procedure:** Any one of the following procedures aimed at improving cardiac status ***(Mark all that apply.)***

☐ 1 Coronary artery bypass graft (CABG)
☐ 2 Percutaneous transluminal coronary angioplasty (PTCA), coronary stent, or coronary atherectomy

6.3. Second myocardial infarction (MI) (i.e., second MI <u>not</u> already reported in Question 4) occurring as a result of or during the revascularization procedure. ***(Mark one.)***

☐ 0 No
☐ 1 Yes
☐ 2 Unknown

WHI **Form 121 - Report of Cardiovascular Outcome** **Ver. 8.1**

Yes ☐1 No ☐0 **7. Carotid artery disease requiring and/or occurring during hospitalization.** Disease must be **symptomatic and/or requiring intervention** (i.e., vascular or surgical procedure).

7.1. Date of Admission: ___ - ___ - ___ (M/D/Y)

7.2. Diagnosis: ***(Mark one.)***

- ☐1 Carotid artery occlusion and stenosis without documentation of cerebral infarction
- ☐2 Carotid artery occlusion and stenosis with documentation of cerebral infarction

7.3. **Carotid artery disease based on** (Hospitalization plus one or more of the following): ***(Mark all that apply.)***

- ☐1 Symptomatic disease with carotid artery disease listed on the hospital discharge summary
- ☐2 Symptomatic disease with abnormal findings (≥ 50% stenosis) on carotid angiogram, MRA, or Doppler flow study
- ☐3 Vascular or surgical procedure to improve flow to the ipsilateral brain

Yes ☐1 No ☐0 **8. Peripheral arterial disease (aorta, iliac arteries, or below) requiring and/or occurring during hospitalization.** Symptomatic disease including intermittent claudication, ischemic ulcers, or gangrene. Disease must be **symptomatic and/or requiring intervention** (e.g., vascular or surgical procedure for arterial insufficiency in the lower extremities or abdominal aortic aneurysm).

8.1. Date of Admission: ___ - ___ - ___ (M/D/Y)

8.2. Diagnosis: ***(Mark the one category that applies best.)***

- ☐1 Lower extremity claudication
- ☐2 Atherosclerosis of arteries of the lower extremities
- ☐3 Arterial embolism and/or thrombosis of the lower extremities
- ☐4 Abdominal aortic aneurysm (AAA)

8.3. **Peripheral arterial disease based on:** Defined by hospitalization plus one or more of the following: ***(Mark all that apply.)***

- ☐1 Ultrasonographically- or angiographically-demonstrated obstruction, or ulcerated plaque (≥ 50% of the diameter or ≥ 75% of the cross-sectional area) demonstrated on ultrasound or angiogram of the iliac arteries or below
- ☐2 Absence of pulse by doppler in any major vessel of lower extremities
- ☐3 Exercise test that is positive for lower extremity claudication
- ☐4 Surgery, angioplasty, or thrombolysis for peripheral arterial disease
- ☐5 Amputation of one or more toes or part of the lower extremity because of ischemia or gangrene
- ☐6 Exertional leg pain relieved by rest and at least one of the following: (1) claudication diagnosed by physician, or (2) ankle-arm systolic blood pressure ratio ≤ 0.8
- ☐7 Ultrasonographically- or angiographically-demonstrated abdominal aortic aneurysm
- ☐8 Surgical or vascular procedure for abdominal aortic aneurysm

_____
Responsible Adjudicator Signature

WHI **Form 121 - Report of Cardiovascular Outcome** **Ver. 8.1**

Table 1
Definition of Criteria for Diagnosis of Myocardial Infarction

	Cardiac Enzyme Interpretation (see *Table 8.8* below)			
	Abnormal	**Equivocal**	**Incomplete**	**Normal**
ECG Pattern/Symptoms				
Cardiac pain present:				
Evolving Q wave and evolving ST-T abnormalities	Definite MI	Definite MI	Definite MI	Definite MI
Equivocal Q wave evolution; or evolving ST-T abnormalities, or new left bundle branch block	Definite MI	Definite MI	Probable MI	No MI
Q waves or ST-T abnormalities suggestive of an MI and not classified above	Definite MI	Probable MI	No MI	No MI
Other ECG, ECG absent or uncodable	Definite MI	No MI	No MI	No MI
Cardiac Pain absent:				
Evolving Q wave and evolving ST-T abnormalities	Definite MI	Definite MI	Definite MI	Probable MI
Equivocal Q wave evolution; or evolving ST-T abnormalities; or new left bundle branch block	Definite MI	Probable MI	No MI	No MI
Q waves or ST-T abnormalities suggestive of an MI and not classified above	Probable MI	No MI	No MI	No MI
Other ECG, ECG absent or uncodable	No MI	No MI	No MI	No MI

Table 2
Algorithm for Enzyme Diagnostic Criteria

		Interpretation	
Cardiac Enzyme	**Abnormal***	**Equivocal**	**Normal**
Creatine kinase MB fraction (CK-MB)	≥ 2x ULN (as %, index, or units); or "present" without quantification	1-2x ULN (as %, index, or units); or "weakly present"	WNL
Toponin (C, I, or T)**	Troponin ≥ 2x ULN	Troponin 1-2x ULN	Troponin is WNL
Total creatine kinase (CK) (no MB available)	N/A	Total CK ≥ 2x ULN	Total CK is 1-2x ULN or WNL

ULN = upper limit of normal
WNL = within normal limits

* If both CK-MB and Troponin are available, Troponin must be elevated to be considered abnormal, if only CK-MB is available, abnormal levels are enough to code enzymes as abnormal, i.e., WHI considers Troponin as the most accurate indicator of myocardial injury.

** Code Troponin levels using the ULN and not Upper limit of undeterminate/indecisive as the reference value. Thus, if 2 cut points are given, choose the lower cut point for the ULN.

8.8.6 Form 132 – Report of Stroke Outcomes

This form must be completed to confirm a stroke or hospitalized carotid artery disease. Self report of a TIA that results in a hospital stay of 2 nights or more is also adjudicated for a possible missed stroke.

Administrative Questions

Date Completed: Date the Physician Adjudicator completed the form.

Adjudicator Code: 5-digit ID for the Physician Adjudicator.

Central Case No.: Case number assigned by WHIX.

Case Copy No.: Copy number assigned by WHIX.

Qx. 1 – Stroke

Stroke is defined as the rapid onset of a persistent neurologic deficit attributed to an obstruction or rupture of the brain arterial system (including stroke occurring during or resulting from a procedure). The deficit is not known to be secondary to brain trauma, tumor, infection, or other cause. The deficit must last more than 24 hours unless death supervenes **or** there is a demonstrable lesion compatible with an acute stroke on CT or MRI. A stroke is defined as procedure-related if it occurs within 24 hours after any procedure or within 30 days after a cardioversion or invasive cardiovascular procedure.

The diagnosis of stroke will be made by the Stroke Adjudicators based on medical records documentation demonstrating that a stroke has occurred. WHI Extension Study strokes will include those occurring during surgery or procedures, those aborted by thrombolytic therapy (streptokinase, TPA, etc.), and those occurring in the outpatient setting. Central retinal artery infarction is also classified as a stroke.

The definition of a stroke **excludes**:

- Headache alone and no demonstrated blood by lumbar puncture, CT, or MRI scan.
- Bell's palsy or labyrinthine disease.
- Metabolic problems (such as diabetic, uremic, or hepatic coma) as a cause of altered consciousness.
- Brain tumor as found or diagnosed by hospital course, CT or MRI scan, angiography, biopsy, or autopsy.
- Trauma as diagnosed by history, CT or MRI scan, or angiography.
- Infection (encephalitis, abscess) as diagnosed by CT or MRI scan, lumbar puncture, or absence of fever.
- Old stroke by CT or MRI scan. This is usually diagnosed if the location of the infarct is inappropriate to explain the findings or when there is nearby focal ventricular enlargement. Recent infarcts often have edema or show distortion of the brain, are enhanceable, or show progression between serial CT or MRI scans.
- Seizures with status and post-ictal paralysis (Todd's) ruled out by history or observation **and** history of past seizures. Sometimes when a stroke causes seizure, CT or MRI scan or angiogram can confirm the stroke.
- Venous infarcts and epidural and subdural hematomas (including those documented as non-traumatic).
- Hysteria, which can usually be differentiated by inconsistencies on examination and evidence of secondary gain.

Qx. 1.1 – Date of admission or diagnosis

The **admit date** on the hospital or outpatient medical records.

Qx. 1.2 – Diagnosis

Stroke outcomes will be divided into 3 subtypes: **Hemorrhagic**, **Ischemic**, and **Other**. Mark the one category that corresponds best to the Stroke Adjudicator's final diagnosis.

Stroke Terminology and Definitions

Rapid onset: Symptoms arising within minutes to hours and occasionally days. Symptoms that progress for more than 1 week are less likely to be associated with stroke.

Mottling: High density (blood) within a low density infarction.

Bloody Cerebral Spinal Fluid (CSF): A non-traumatic lumbar puncture positive for subarachnoid hemorrhage with > 100 cells/mm^3. Counts in the last tube are similar to those in the first tube (no clearing) or xanthochromia is present when the specimen is spun down.

Focal neurologic deficit: Signs/symptoms localized to one or a few locations.

Compatible with: Can explain the neurologic deficit.

Hemorrhagic Stroke (codes 1-3)

Hemorrhagic stroke is categorized into the following three categories:
- Subarachnoid hemorrhage (code 1)
- Intraparenchymal hemorrhage (code 2)
- Other or unspecified hemorrhage intracranial (e.g., isolated intraventricular hemorrhage) (code 3)

A diagnosis of hemorrhagic stroke requires one of the following criteria:
- Blood in subarachnoid space or intraparenchymal hemorrhage by CT or MRI scan. (Intraparenchymal blood must be dense and not mottled--mixed hyperdensity and hypodensity.)
- **Or** bloody spinal fluid by lumbar puncture plus neurologic signs and symptoms consistent with stroke.
- **Or** death from stroke within 24 hours of symptom onset **and** no lumbar puncture, CT or MRI scan, or autopsy is available. (Death within 24 hours of onset of stroke is nearly always due to hemorrhage.)
- **Or** surgical or autopsy evidence of hemorrhage as the cause of a clinical syndrome consistent with a stroke.

Ischemic Stroke (code 4): Occlusion of cerebral or pre-cerebral arteries with infarction (cerebral thrombosis, cerebral embolism, lacunar infarction)

A diagnosis of stroke due to ischemic infarction requires one of the following criteria:
- Focal neurologic deficit without CT or MRI scan, lumbar puncture, or evidence of blood.
- **Or** CT or MRI scan with mottled cerebral pattern or showing decreased density in a location compatible with reported symptoms and signs.
- **Or** Surgical or autopsy evidence of ischemic infarction (cerebral thrombosis or cerebral embolism).

Other (code 5): Acute, but ill-defined, cerebrovascular disease (select this option only if unable to code as hemorrhagic or ischemic)
- Inadequate information to categorize as hemorrhagic or ischemic infarction, but satisfies criteria for stroke.

Qx. 1.3 – Stroke during or resulted from a procedure

Stroke occurred or resulted from a procedure within 24 hours after any procedure or within 30 days after a cardioversion or invasive cardiovascular procedure. Mark one response.

Qx. 1.4 – Diagnosed or managed as outpatient

The outpatient setting includes any emergency department or observation unit admission, short stays of less than 24 hours duration, or a direct admission to a rehab facility without an associated admission to an acute care hospital.

Qx. 1.5 – Oxfordshire Classification

Total anterior circulation infarct (TACI): Must have all 3 components

Artery: Internal carotid artery or middle cerebral artery stem.

Clinical Features:

1) Combination of higher cerebral dysfunction	• Aphasia • Dyscalculia • Visuospatial dysfunction • Neglect
2) Visual defect	• Homonymous hemianopsia
3) Motor or sensory deficit	• Ipsilateral motor deficit (at least 2 areas involved, face, arm, leg) • Ipsilateral sensory deficit (at least 2 areas involved, face, arm, leg)

Partial anterior circulation infarct (PACI): Must meet one of the following 3 criteria (1-3) in a participant with no drowsiness, or 4 or 5.

Artery: Internal carotid artery, middle cerebral artery stem, or branch, anterior cerebral artery

Clinical Features: 2 of 3 criteria of total anterior circulation infarction (TACI)

1) New higher cerebral dysfunction	• Dysphasia • Dyscalculia • Visuospatial dysfunction • Neglect
2) Visual defect	• Homonymous hemianopsia
3) Motor and/or sensory deficit	• Ipsilateral motor deficit • Ipsilateral sensory deficit

or 4) Higher cerebral dysfunction alone (e.g., dysphasia)

or 5) Motor/sensory deficit more restricted than those classified as Lacunar Syndrome (LACI), e.g., confined to one limb

Lacunar infaction (LACI): Must have all 3 components.

Artery: Occlusion of a small deep perforating artery

Clinical Features:

1) Lacunar syndrome - Any of the following:	• Pure motor stroke (2 of 3 areas must be involved, face, arm, leg) • Pure sensory stroke (2 of 3 areas must be involved, face, arm, leg) • Sensory-motor stroke (2 of 3 areas must be involved, face, arm, leg) • Ataxic hemiparesis
2) Absence of cortical deficit	
3) Absence of brainstem signs	

Posterior circulation infarct (POCI): Any of the following:

Artery: Vertebral, basilar or posterior cerebral artery

Clinical Features:

- Ipsilateral cranial nerve deficit and contralateral motor deficit
- Ipsilateral cranial nerve deficit and contralateral sensory deficit
- Bilateral motor deficit
- Bilateral sensory deficit
- Disorder of conjugate eye movement
- Cerebellar dysfunction
- Isolated homonymous visual defect

Qx. 1.6 – TOAST Classification

Mark the one category that applies best (from: Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification).

Probable vs. Possible categories

- A "probable" diagnosis is made if the clinical findings, neuroimaging data, and results of diagnostic studies are consistent with one subtype and other etiologies have been excluded.
- A "possible" diagnosis is made when the clinical findings and neuroimaging data suggest a specific subtype but other studies are not done.

Large artery atherosclerosis (embolus/thrombosis) – Codes 1 and 5

Mark if any of the following are reported:

- Carotid lesions greater than 50% stenosis and ipsilateral to the lesion
- Vertebral lesions are relevant only in cases of brain stem infarction

Cardioembolism (high-risk/medium risk)– Codes 2 and 6

Mark if any of the following are reported:

- Mechanical prosthetic heart valve
- Atrial fibrillation
- Sick-sinus syndrome
- Myocardial infarction (MI) within 4 weeks: as stated
- Dilated cardiomyopathy: as stated per history
- Atrial myxoma: as described by studies prior to admission (usually echocardiogram)
- Infective endocarditis
- Akinetic left ventricular segment
- Left ventricular thrombus: Score this item if at any time in the patient's history they were found to have a thrombus in the left ventricle. Score even if the patient has completed their recommended course of anticoagulation or if currently taking anticoagulants. Score even if echocardiogram on current admission fails to find thrombus.
- MI > 4 weeks ago but < 6 months ago: as documented in the medical record or by prior WHI adjudication
- Congestive heart failure: Score if recorded in patient's history at any time. Score regardless of patient's current medication regimen or echocardiographic findings on present admission.
- Left ventricular aneurysm: as recorded in history
- Atrial flutter: Score if this rhythm recorded at any time. Score even if the patient is being treated with anticoagulation (e.g., coumadin), antiarrhythmics (e.g., digoxin, calcium channel blockers, beta-blockers), has a pacemaker, or has been successfully undergone cardioversion in the past
- Bioprosthetic heart valve: Score as recorded in patient's history
- Mitral stenosis without atrial fibrillation: as recorded in history and/or current echocardiogram
- Mitral valve prolapse: as recorded in history and/or current echocardiogram
- Mitral annular calcification: as recorded in history and/or current echocardiogram
- Atrial septal defect: as recorded in history. Do NOT record if patient has undergone surgical closure of defect
- Patent foramen ovale: as recorded in history or prior/current echocardiogram
- Interatrial septal aneurysm: as recorded in history or prior echocardiograms
- Nonbacterial endocarditis: as recorded in history. This would include marantic or Libman-Sacks endocarditis

Small vessel occlusion (lacune) – Codes 3 and 7

Mark if any of the following are reported:

- Pure motor (hemiparesis/hemiplegia): New onset weakness of the face, arm and leg. All should be involved on the same side of the body, usually but not always to the same degree. Dysarthria is frequently present. Sensory findings and poor coordination inappropriate for muscle weakness should not be present.
- Pure Sensory: New onset sensory findings occurring on one side of the body, involving at least two of our three body areas (face, arm, leg). Objective findings of sensory loss are not required--sensory symptoms (e.g., numbness) in the above noted distributions qualify. Motor and cerebellar findings should be absent.
- Mixed sensorimotor: Motor and sensory findings simultaneously located in at least 2 out of 3 body areas (face, arm and leg). Tongue deviation and dysarthria may be present.
- Ataxic Hemiparesis: Ipsilateral cerebellar ataxia and hemiparesis. Gait ataxia may be present, and the presence or absence of sensory findings on the same side of the body is variable. The face need not be involved, and arm and leg may be weak to varying extents.
- Dysarthria-Clumsy hand: Severe dysarthria, clumsy ataxic hand (especially on writing); facial weakness; tongue deviation may or may not be present, as may ipsilateral hyper-reflexia and Babinski sign.

Stroke of <u>other</u> determined etiology – Codes 4 and 10

Mark if any of the following are reported:

Activated protein C resistance (e.g. Factor V Leiden)
Amyloid angiopathy
Anticardiolipin antibody
Aortic arch atheroma
Arterial dissection
Behcet's syndrome
CADASIL
Cardiac procedure (post operative)
Churg-Strauss syndrome
Coagulation factor deficiencies: Antithrombin III, protein C, protein S, plasminogen, factor VIII (hemophilia), factor XII, C2, Prekallikrein, heparin cofactor II)
Congenital connective tissue disorders
Cryoglobulinemia
Degos-Kohlmeier Disease
Disseminated intravascular coagulation
Dolichoectasia
Drug induced (amphetamine, cocaine, heroin, LSD, PCP, ecstasy)
Drug induced vasculitis
Eale's disease
Ehler's-Danlos syndrome
Essential thrombocythemia
Fabry's Disease
Fibromuscular dysplasia
Granulomatous angiitis of the CNS
Hematologic
Hemoglobin SC disease
Herpes encephalitis
HIV
Homocysteinemia
Lupus anticoagulant
Malaria
Marfan's syndrome
MELAS
Moya moya
Mucormycoses
Mycoses
Myeloproliferative disorders
Neoplastic angioendotheliosis
Neuroborreliosis (Lyme disease)
Neurobrucellosis
Neurosarcoidosis
Neurosyphilis
Neurotuberculosis
Oral contraceptive induced hypercoagulability
Osler Weber Rendu Syndrome
Other non-inflammatory vasculopathies
Paraneoplastic syndrome
Paroxysmal nocturnal hemoglobinuria
Platelet hyperaggregability
Polyarteritis nodosa
Polycythemia rubra vera
Post-irradiation vasculopathy
Pseudoxanthoma elasticum
Relapsing polychondritis
Rickettsioses (e.g., Rocky Mountain Spotted Fever)
Schistosomiasis
Scleroderma
Severe Anemia
Sickle cell disease
Sjogen's syndrome
Sneddon's syndrome
Systemic lupus erythematosus
Takayasu's disease
Thalassemias
Thrombotic thrombocytopenic purpura (TTP)
Trichinosis
Typhus
Vasospasm
Venous sinus thrombosis
Vitamin K therapy
Waldenstrom's macroglobulinemia
Wegener's granulomatosus

Stroke of <u>undetermined</u> etiology

- Two or more causes identified – Code 11
- Negative evaluation – Code 12
- Incomplete evaluation – Code 13

To be a complete evaluation, the following 3 areas must be evaluated.

1) Neuroimaging
   - CT scan
   - MRI scan
2) Carotid evaluation (any of the following) [a complete evaluation of the relevant arterial distribution, e.g., carotid, vertebral, basilar system]
   - Carotid Dopplers
   - MRA
   - Cerebral angiography
3) Cardiac evaluation
   - Transthoracic Echocardiogram
   - Transesophageal Echocardiogram

Qx. 1.7 – Stroke diagnosis based on criteria

Mark the one category that applies best

- Rapid onset of neurological deficit and CT or MRI scan shows acute focal brain lesion consistent with neurological deficit and without evidence of blood (except mottled cerebral pattern) (code 1)
- Rapid onset of localizing neurological deficit with duration ≥ 24 hours but imaging studies are not available (code 2)
- Rapid onset of neurological deficit with duration ≥ 24 hours and the only available CT or MRI scan was done early and shows no acute lesion consistent with the neurologic deficit (code 3)
- Surgical evidence of ischemic infarction of brain (code 4)
- CT or MRI findings of blood in subarachnoid space, intra-parenchymal, or intraventricular hemorrhage consistent with neurological signs or symptoms (code 5)
- Positive lumbar puncture (for subarachnoid hemorrhage) (code 6)
- Surgical evidence of subarachnoid or intra-parenchymal hemorrhage as the cause of a clinical syndrome consistent with stroke (code 7)
- None of the above (e.g., fatal strokes where no imaging studies or clinical evidence are available; or CT/MRI does not show lesion consistent with the neurologic deficit (code 8)

Qx. 1.8 – If stroke fatal

Mark all that apply. Complete *Form 124 – Report of Death (Final)*. Indicate on the IDS Report that the death needs to be adjudicated by the CVD Adjudicator.

- Hospitalized stroke within 28 days of death (code 1)
- Previous stroke and no known potentially lethal non-cerebrovascular disease process (code 2)
- Stroke diagnosed as cause of death at post-mortem examination (code 3)
- Stroke listed as underlying cause of death on death certificate (code 4)

Occasionally, the death certificate is the only available document. In this case, code the underlying cause as mentioned on the death certificate. If the cause of death is incorrectly ordered on the death certificate, the physician adjudicator may code according to what he/she thinks should be the sequence of events leading to death. In instances where this is the only documentation available it should be considered the most accurate determination of the cause of death.

- It is possible to code Box 1 – Hospitalized stroke with 28 days of death without checking Box 4 – Stroke listed as the underlying cause of death (COD) [e.g., the immediate or a contributory COD].
- Box 4 – Stroke listed as the underlying COD on the death certificate is not required to be checked in order to mark Qx. 1.9 – Functional Status, Box 5 – Dead.

Qx. 1.9 – Participant's functional status at time of discharge (Glasgow Outcome Scale)

Mark the one category that applies best. Complete the Glasgow Outcome Scale at the time of discharge from the medical service, using only current medical records documentation provided in the

case packet. The participant may be discharged from the Emergency Department, hospital, or physician's office. Do not request additional medical records to determine the Glasgow Outcomes Scale. If, based on currently available medical records, you are unable to categorize the participant, mark Box 6 – "Unable to categorize participant based on available case packet documentation." (For limited use only when adjudicator is unable to otherwise categorize.)

- Good recovery – Participant can lead a full and independent life with or without minimal neurological deficit. Participant should have a normal neurological examination or a single neurological deficit (code 1)
- Moderately disabled – Participant has neurological or intellectual impairment but is independent. Participant has neurological deficit but does not rely on others for activities of daily living (code 2)
- Severely disabled – Participant conscious but dependent on others to get through daily activities (code 3)
- Vegetative survival – Participant has no obvious cortical functioning. Participant may have eye opening, reactive pupils, limb movement, decorticate or decerebrate posturing, and semi-purposeful movements, but there is no purposeful avoidance of/withdrawal from painful stimuli (code 4)
- Dead (code 5)
- Unable to categorize stroke based on available case packet documentation (for limited use only when adjudicator is unable to categorize above) (code 6)

Qx. 2 – Transient Ischemic Attack (TIA)

Transient ischemic attack is defined as the rapid onset of a neurologic deficit attributed to an embolus or an obstruction of the arterial system that is not known to be secondary to brain trauma, tumor, infection, or other cause. In the WHI Extension Study, TIA is only collected by self-report on *Form 33* (i.e., the report of TIA does not require procurement of medical records). However, in instances where the self-report of TIA results in a hospitalization of 2 nights or more or a report of stroke is denied by the CCC Stroke Adjudicator and determined to be a TIA based on the criteria below, a *Form 132 – Report of Stroke Outcome* is completed.

Yes/No. Mark the appropriate box and complete Question 2.1 if the participant has evidence of TIA. Mark "Yes" for a report of an acute neurologic event that does not satisfy the definition of a stroke but satisfies the definition given for a TIA.

A participant has a diagnosis of TIA if she has one or more episodes of a focal neurologic deficit lasting more than 30 seconds and no longer than 24 hours in the absence of head trauma immediately preceding the onset. There must have been rapid evolution of the symptoms to the maximal deficit in less than 5 minutes with complete resolution within 24 hours. There should be no evidence of clonic jerking, conjugate eye deviation, prolonged Jacksonian march, scintillating scotoma, or headache with nausea and vomiting. Conditions to be ruled out include seizures, hypoglycemia, migraine, drug intoxication, tumor, infection, orthostatic hypotension, and generalized cerebral ischemia. Discovery of an infarct by CT or MRI scan in a location compatible with the symptoms, even if the symptoms cleared in less than 24 hours, shall be diagnosed as a stroke, not a TIA.

Disorders not typically considered TIA:

- March of a sensory deficit
- Vertigo alone
- Dizziness alone
- Dysphagia alone
- Dysarthria alone
- Diplopia alone
- Incontinence of bowel or bladder
- Loss of vision associated with alteration of level of consciousness
- Focal symptoms associated with migraine
- Confusion alone
- Amnesia alone
- Drop attacks alone
- Unconscious without other signs of posterior circulation symptoms
- Tonic or clonic activity
- Prolonged march of symptoms over several areas of the body
- Scintillating scotoma

There must be clear and convincing evidence to diagnose TIA in individuals with these symptoms, otherwise individuals with these symptoms should be classified not TIA. (Reference: Classification of cerebrovascular diseases III. Stroke 21: 637-676, 1990.)

Qx. 2.1 – Date of Admission or Diagnosis

The hospital admit date or date of diagnosis on the outpatient medical records.

Qx. 3 – Carotid Artery Disease requiring Hospitalization

Yes/No. Mark the appropriate box and complete Question 3.1 to 3.3 to confirm the carotid artery disease. Note the participant must be hospitalized (and symptomatic or requiring intervention).

Qx. 3.1 – Date of Admission

The admit date on the medical records.

Qx. 3.2 – Diagnosis

Mark the one box that corresponds best to the Physician Adjudicator's final diagnosis.

- Carotid artery occlusion and stenosis without documentation of cerebral infarction (code 1)
- Carotid artery occlusion and stenosis with written documentation of cerebral infarction (code 2)

Qx. 3.3 – Carotid artery disease base on (criteria)

Mark all that apply. Note the participant must be hospitalized (and symptomatic or requiring intervention).

- Symptomatic disease with carotid artery disease listed on the hospital discharge summary (code 1)
- Symptomatic disease with abnormal findings (≥ 50% stenosis) on carotid angiogram, MRA, or doppler flow study (code 2)
- Vascular or surgical procedure to improve flow to the ipsilateral brain (code 3)

Responsible Adjudicator Signature

The Physician Adjudicator should sign the form only when s/he is satisfied that the questions on the cardiovascular outcomees being reported have been filled in as completely and accurately as possible on the basis of all available information, and that other outcomes (e.g., hospitalization) have been investigated and adjudicated.

Figure 8.5
Form 132 – Report of Stroke Outcome

WHI **Form 132 - Report of Stroke Outcome** **Ver. 8.2**

OMB #0925-0414 Exp: 5/09

COMMENTS	**-Affix label here-** Member ID: __ __ __ __ - __ __ __ __ - __
To be completed by Physician Adjudicator. Date Completed: ___-___-___ (M/D/Y) Adjudicator Code: ___-___	Central Case No.: _____ Case Copy No.: ___

Yes **No**
☐1 ☐0 **1.** **Stroke:** Rapid onset of a persistent neurologic deficit attributable to an obstruction or rupture of the arterial system (including stroke occurring during **or resulting from** a procedure).* Deficit is not known to be secondary to brain trauma, tumor, infection, or other cause. Deficit must last more than 24 hours, unless death supervenes or there is a demonstrable lesion compatible with acute stroke on CT or MRI scan.

*A stroke is defined as procedure-related if it occurs within 24 hours after any procedure or within 30 days after a cardioversion or invasive cardiovascular procedure.

1.1. Date of Admission or diagnosis: ___-___-___ (M/D/Y)

1.2. Diagnosis: ***(Mark the one category that applies best.)***

Hemorrhagic Stroke

☐1 Subarachnoid hemorrhage

☐2 Intraparenchymal hemorrhage

☐3 Other or unspecified intracranial hemorrhage (e.g., isolated intraventricular hemorrhage)

Ischemic Stroke ***(If selected, complete questions 1.5 – Oxfordshire and 1.6 - TOAST Classification on the next page.)***

☐4 Occlusion of cerebral or pre-cerebral arteries with infarction (cerebral thrombosis, cerebral embolism, lacunar infarction)

Other

☐5 Acute, but ill-defined, cerebrovascular disease (select this option only if unable to code as hemorrhagic or ischemic)

1.3. Stroke occurred during or resulted from a procedure (defined above*). **(Mark one.)**

☐0 No

☐1 Yes

☐9 Unknown

1.4. Was the stroke diagnosed or managed as an outpatient?*

☐0 No

☐1 Yes

*The outpatient setting includes any emergency department or observation unit, short hospital stays of less than 24 hours duration or a direct admission to a rehab facility without an associated admission to an acute care hospital.

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Figure 8.5 (continued)
Form 132 – Report of Stroke Outcome

WHI **Form 132 - Report of Stroke Outcome** **Ver. 8.2**
OMB #0925-0414 Exp: 5/09

1.5. Oxfordshire Classification ***(Mark the <u>one</u> category that applies best.)***

- ☐ 1 Total anterior circulation infarct (TACI)
- ☐ 2 Partial anterior circulation infarct (PACI)
- ☐ 3 Lacunar infarction (LACI)
- ☐ 4 Posterior circulation infarct (POCI)

1.6. Trial of Org 10172 in Acute Stroke Treatment (TOAST) Classification
(Mark the <u>one</u> category that applies best.)

	Probable	Possible
Large artery atherosclerosis (embolus/thrombosis)	☐ 1	☐ 5
Cardioembolism (high-risk/medium risk)	☐ 2	☐ 6
Small vessel occlusion (lacune)	☐ 3	☐ 7
Stroke of other determined etiology	☐ 4	☐ 10
Stroke of undetermined etiology		
Two or more causes identified	☐ 11	
Negative evaluation	☐ 12	
Incomplete evaluation	☐ 13	

1.7 Stroke diagnosis based on: ***(Mark the <u>one</u> category that applies best.)***

- ☐ 1 Rapid onset of neurological deficit and CT or MRI scan shows acute focal brain lesion consistent with neurological deficit and without evidence of blood (except mottled cerebral pattern)
- ☐ 2 Rapid onset of localizing neurological deficit with duration ≥ 24 hours but imaging studies are not available
- ☐ 3 Rapid onset of neurological deficit with duration ≥ 24 hours and the only available CT or MRI scan was done early and shows no acute lesion consistent with the neurologic deficit
- ☐ 4 Surgical evidence of ischemic infarction of brain
- ☐ 5 CT or MRI findings of blood in subarachnoid space, intra-parenchymal, or intraventricular hemorrhage consistent with neurological signs or symptoms
- ☐ 6 Positive lumbar puncture (for subarachnoid hemorrhage)
- ☐ 7 Surgical evidence of subarachnoid or intra-parenchymal hemorrhage as the cause of a clinical syndrome consistent with stroke
- ☐ 8 None of the above (e.g., fatal strokes where no imaging studies or clinical evidence are available; or CT/MRI does not show lesion consistent with the neurologic deficit)

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Figure 8.5 (continued)
Form 132 – Report of Stroke Outcome

WHI **Form 132 - Report of Stroke Outcome** **Ver. 8.2**
OMB #0925-0414 Exp: 5/09

1.8. If stroke fatal: ***(Mark all that apply.)***

☐1 Hospitalized stroke within 28 days of death

☐2 Previous stroke and no known potentially lethal non-cerebrovascular disease process

☐3 Stroke diagnosed as cause of death at post-mortem examination

☐4 Stroke listed as underlying cause of death on death certificate

1.9 Participant's functional status at the time of discharge* (Glasgow Outcome Scale):
(Mark the <u>one</u> category that applies best.)
*Participant may be discharged from the Emergency Department, hospital, or physician's office.

☐1 Good recovery – Patient can lead a full and independent life with or without minimal neurological deficit

☐2 Moderately disabled – Patient has neurological or intellectual impairment but is independent

☐3 Severely disabled – Patient conscious but dependent on others to get through daily activities

☐4 Vegetative survival – Has no obvious cortical functioning

☐5 Dead

☐6 Unable to categorize stroke based on available case packet documentation (for limited use only when adjudicator is unable to categorize above).

Yes ☐1 **No** ☐0 **2.** **Transient ischemic attack:** One or more episodes of a focal neurologic deficit lasting more than 30 seconds and no longer than 24 hours. Rapid evolution of the symptoms to the maximal deficit in less than 5 minutes, with subsequent complete resolution. No head trauma occurring immediately before the onset of the neurological event.

2.1. Date of Admission or diagnosis: ___ - ___ - ___ (M/D/Y)

Yes ☐1 **No** ☐0 **3.** **Carotid artery disease requiring and/or occurring during hospitalization.** Disease must be **symptomatic and/or requiring intervention** (i.e., vascular or surgical procedure).

3.1. Date of Admission: ___ - ___ - ___ (M/D/Y)

3.2. Diagnosis: ***(Mark one.)***

☐1 Carotid artery occlusion and stenosis without documentation of cerebral infarction

☐2 Carotid artery occlusion and stenosis with written documentation of cerebral infarction

3.3. **Carotid artery disease based on** (Hospitalization <u>plus</u> one or more of the following):
(Mark all that apply.)

☐1 Symptomatic disease with carotid artery disease listed on the hospital discharge summary

☐2 Symptomatic disease with abnormal findings (≥ 50% stenosis) on carotid angiogram, MRA, or Doppler flow study

☐3 Vascular or surgical procedure to improve flow to the ipsilateral brain

_____
Responsible Adjudicator Signature

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8.9 Other Outcomes (Excluding Fractures and Cancer)

Other outcomes adjudicated for WHI Extension Study include venous thromboembolic disease and hysterectomy, both adjudicated only for previous HT participants. Data on these conditions for other WHI Extension Study participants is collected by self-report only.

8.9.1 Form 126 – Report of Venous Thromboembolic Disease (HT)

Venous thromboembolic includes both 1) deep vein thrombosis, either hospitalized or managed as an outpatient and 2) pulmonary embolism requiring hospitalization. Both are adjudicated only for HT participants using *Form 126 – Report of Venous Thromboembolic Disease (HT)*.

Administrative Questions

Date Completed: Date the Physician Adjudicator completed the form.

Adjudicator Code: 5-digit ID for the Physician Adjudicator.

Central Case No.: Case number assigned by WHIX.

Case Copy No.: Copy number assigned by WHIX.

Qx. 1 – Deep Vein Thrombosis (DVT)

The presence of thrombus within a deep vein and the accompanying inflammatory response in vessel wall is termed deep vein thrombosis. In the WHI Extension Study, only deep vein thrombosis of the lower extremity, pelvis, or IVC is of interest. Deep vein thrombosis in other locations such as the upper extremity is not adjudicated.

Qx. 1.1 – Date of Diagnosis/Admission

If hospitalized DVT, the admit date on the hospital medical records.
If outpatient DVT, the date of the procedure or test that first diagnosed the DVT.

Qx. 1.2 – Diagnosis

Mark the one category that corresponds best to the Physician Adjudicator's final diagnosis.

- DVT of lower extremities not resulting from a procedure within 60 days (code 1)
- DVT of lower extremities during or following a procedure within 60 days (code 2)

Qx. 1.3 – Diagnosis based on

Mark all that apply. The diagnosis of DVT can be made when the diagnosis is present in the discharge summary (code 1) **or any** of the following are recorded:

- Positive findings on a venogram, defined as presence of a filling defect (code 2)
- Positive findings using impedance plethysmography, indicating a flow defect (code 3)
- Positive findings on doppler duplex examination, ultrasound, sonogram, or other non-invasive test examination, demonstrating a flow velocity disturbance (code 4)
- Positive findings on isotope scan (e.g., I^{125} fibrinogen scan) (code 5)

Qx. 1.4 – Diagnosis Reporting Source

Mark one. The categories are listed in hierarchical order - if more than one category applies, mark the first applicable category.

- Hospital inpatient
- Hospital outpatient facility or clinic
- Radiology or imaging facility
- Physician's office/private medical practitioner

- Nursing/convalescent home/hospice
- Autopsy only
- Death Certificate only
- Other

Qx. 1.5 – Work-up for PE performed

Mark one: yes, no, unknown.

Qx. 2 – Pulmonary embolism (PE) requiring hospitalization

Qx. 2.1 – Date of Diagnosis/Admission

The admit date on the hospital medical records.

Qx. 2.2 – Diagnosis

Mark the one category that corresponds best to the Physician Adjudicator's final diagnosis.

- PE not resulting from a procedure within 60 days (code 1)
- PE during or following a procedure within 60 days (code 2)

Qx. 2.3 – Diagnosis based on

Mark all that apply. Pulmonary embolism (PE) is defined as present if one of the following is present:

- Pulmonary embolism reported as a diagnosis in the discharge summary (code 1)
- Report of a positive findings on appropriate diagnostic studies (code 2), including:
  a) Pulmonary ventilation/perfusion (V/Q) report describing a "high" probability of deficit. Moderate, intermediate, or low probability on a V/Q lung scan will not be considered confirmation of a PE
  b) Pulmonary angiography report or spiral CT describing either "cut off" of a vessel or "filling defect" (code 3)
- Diagnosis of deep vein thrombosis (DVT) based on ≥ 1 DVT criteria (see *Section 8.9.1.1 – Deep Vein Thrombosis*) plus signs and symptoms of PE (i.e., acute chest pain, dyspnea, tachypnea, hypoxemia, tachycardia, or chest X-ray findings suggestive of PE) (code 4)
- Other, including autopsy (code 8)

Responsible Adjudicator Signature

The Physician Adjudicator should sign the form only when s/he is satisfied that the questions on the DVT and PE are being reported have been filled in as completely and accurately as possible on the basis of all available information, and that other outcomes (e.g., hospitalization) have been investigated and adjudicated.

Figure 8.6
Form 126 – Report of Venous Thromboembolic Disease (HT)

WHI **Form 126 - Report of Venous Thromboembolic Disease (HT)** **Ver. 8.1**

OMB #0925-0414 Exp: 5/09

COMMENTS	**-Affix label here-** Member ID: __ __ __ __ - __ __ __ __ - __
To be completed by Physician Adjudicator: Date Completed: ___-___-___ (M/D/Y) Adjudicator Code: ___-___	Central Case No.: _____ Case Copy No.: ___

Complete this form only if the participant is in the Hormone Trial (HT) component.

Yes ☐1 No ☐0

1. **Deep vein thrombosis (DVT)**

1.1 Date of Diagnosis/Admission:
___-___-___ (M/D/Y)

1.2 Diagnosis: ***(Mark the one category that applies best.)***

☐1 Deep vein thrombosis of lower extremities **not resulting from a procedure** within 60 days
☐2 Deep vein thrombosis of lower extremities **during or following a procedure** within 60 days

1.3 Diagnosis of deep vein thrombosis is based on: ***(Mark all that apply.)***

☐1 Hospital discharge summary with a diagnosis of deep vein thrombosis
☐2 Positive findings on a venogram
☐3 Positive findings using impedance plethysmography
☐4 Positive findings on doppler duplex, ultrasound, sonogram, or other non-invasive test examination
☐5 Positive findings on isotope scan

1.4 Diagnosis of deep vein thrombosis reporting source: (***Mark one. If more than one category applies, mark the first applicable category.)***

☐1 Hospital inpatient
☐2 Hospital outpatient facility or clinic
☐3 Radiology or imaging facility
☐4 Physician's office/private medical practitioner
☐5 Nursing/convalescent home/hospice
☐6 Autopsy only
☐7 Death Certificate only
☐8 Other

1.5 Was a work up for pulmonary embolism performed?

☐1 Yes ☐0 No ☐8 Unknown

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Figure 8.6 (continued)
Form 126 – Report of Venous Thromboembolic Disease (HT)

WHI **Form 126 - Report of Venous Thromboembolic Disease (HT)** **Ver. 8.1**

Yes ☐1 No ☐0 **Pulmonary embolism (PE) requiring hospitalization:**

2.1 Date of Diagnosis/Admission: ___-___-___ (M/D/Y)

2.2 Diagnosis: ***(Mark the one category that applies best.)***

☐1 Pulmonary embolism **not resulting from a procedure** within 60 days

☐2 Pulmonary embolism **during or following a procedure** within 60 days

2.3 Diagnosis of pulmonary embolism is based on:
(Mark <u>all</u> that apply.)

☐1 Hospital discharge summary with a diagnosis of pulmonary embolism

☐2 High probability on ventilation-perfusion lung scan (exclude moderate, intermediate, or low probability on ventilation-perfusion lung scan)

☐3 Positive findings on pulmonary angiogram or spiral CT

☐4 Diagnosis of deep vein thrombosis (DVT) based on ≥1 DVT criteria in 1.3. plus signs and symptoms suggestive of PE (e.g., acute chest pain, dyspnea, tachypnea, hypoxemia, tachycardia, or chest X-ray findings suggestive of PE)

☐8 Other, including autopsy

_____
Responsible Adjudicator Signature

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8.9.2 Form 131 – Report of Hysterectomy (HT)

Complete this form only for HT participants. Adjudication of hysterectomy includes review of the adjudication case packet (containing face sheet, discharge summary or outpatient report and operative report) to identify:

- Type of hysterectomy – Abdominal or vaginal,
- Associated surgery – Oophorectomies performed,
- Reason for the hysterectomy – Abstraction of narrative information in medical records.

While reviewing the case packet, also determine the possibility of a cancer outcome. If a cancer is identified, request appropriate documents and/or adjudication of the cancer (if appropriate documents have already been obtained). Note that if the participant is hospitalized for the hysterectomy, also review the hospitalization for other outcomes and complete *Form 125 – Summary of Hospitalization Diagnosis*.

Administrative Questions

Date Completed: Date the Physician Adjudicator completed the form.

Adjudicator Code: 5-digit ID for the Physician Adjudicator.

Central Case No.: Case number assigned by WHIX.

Case Copy No.: Copy number assigned by WHIX.

Qx. 1 – Hysterectomy (HT)

Complete this form only for HT participants, and only if a hysterectomy is confirmed. If review of the adjudication packet shows there was no hysterectomy, do not complete the form.

Qx. 1.1 – Date of hysterectomy

Date the hysterectomy was performed.

Qx. 2 – Type of hysterectomy

Mark the one category that applies best:

- Abdominal
- Vaginal

Qx. 3 – Associated surgery

Mark the one category that applies best:

- None (code "0")
- Partial oophorectomy (code 1)
- One ovary removed (code 2)
- Bilateral oophorectomy (code 3)

Qx. 4 – Reason for hysterectomy

Mark the one category that applies best:

- Cancer (code 1)
- Atypical hyperplasia (code 2)
- Bleeding (code 3)
- Fibroids (myomas) (code 4)
- Endometriosis (code 5)
- Descensus (prolapse) (code 6)
- Other (code 8)

Responsible Adjudicator Signature

The Physician Adjudicator should sign the form only when s/he is satisfied that the questions on the cardiovascular outcomes being reported have been filled in as completely and accurately as possible on the basis of all available information, and that other outcomes (e.g., hospitalization) have been investigated and adjudicated.

Figure 8.7
Form 131 – Report of Hysterectory (HT)

WHI **Form 131 - Report of Hysterectomy (HT)** **Ver. 8**

COMMENTS	-Affix label here- Member ID: __ __ __ - __ __ __ __ - __
To be completed by Physician Adjudicator: Date Completed: __-__-__ (M/D/Y) Adjudicator Code: __-__	Central Case No.: __ __ __ __ __ Case Copy No.: __

Complete this form only if the participant is in the Hormone Trial (HT) component.

1. **Hysterectomy (HT only)**

   1.1. Date of hysterectomy: __-__-__ (M/D/Y)

2. Type of hysterectomy: ***(Mark the one category that applies best.)***
   - ☐ 1 Abdominal
   - ☐ 2 Vaginal

3. Associated surgery: ***(Mark the one category that applies best.)***
   - ☐ 0 None
   - ☐ 1 Partial oophorectomy
   - ☐ 2 One ovary removed
   - ☐ 3 Bilateral oophorectomy

4. Reason for hysterectomy: ***(Mark the one category that applies best.)***
   - ☐ 1 Cancer
   - ☐ 2 Atypical hyperplasia
   - ☐ 3 Bleeding
   - ☐ 4 Fibroids (myomas)
   - ☐ 5 Endometriosis
   - ☐ 6 Descensus (prolapse)
   - ☐ 8 Other ***(Specify)***: _____

_____
Responsible Adjudicator Signature

RV_____K_____V_____

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8.10 Fracture Outcomes Adjudication

Hip fractures are a primary outcome of the Calcium and Vitamin D (CaD) trial, and a secondary outcome of the Hormone Trial (HT) and Dietary Modification (DM) trials. In the Women's Health Initiative (WHI) Extension Study, hip fracture is the only type of fracture requiring investigation and adjudication. All other fractures will be collected by self-report on *Form 33 – Medical History Update*.

8.10.1 Fracture Definition

Hip Fracture is defined as a fracture of the proximal femur, including femoral neck, intertrochanteric region, greater trochanter, and other – not specified. See *Figure 8.9 – Fracture of Hip Views*. Hip fracture is the only type of fracture adjudicated in the WHI Extension Study.

Other fractures collected only by self-report on *Form 33* include the following:

- upper leg (not hip)
- pelvis
- knee (patella or tibial plateau)
- lower leg (tibia and/or fibula) or ankle (very distal tibia/fibula and/or talus)
- foot (not toes)
- tailbone (sacrum and/or coccyx)
- spine or back (vertebra)
- lower arm or wrist (radius, ulna, and/or one or more carpal bones)
- hand (not finger) (one or more metacarpal bone[s])
- elbow (lower end of humerus, upper radius and/or ulna)
- upper arm or shoulder (humerus)
- collarbone; all clavicular and scapular fractures
- ribs
- chest/sternum
- skull/face, including nose and jaw
- fingers
- toes
- cervical vertebrae or neck

8.10.2 First vs. Subsequent Report of Hip Fractures

Only the first occurrence of a hip fracture during WHI is investigated and adjudicated. If a participant is hospitalized multiple times for one fracture site, only adjudicate the **first** occurrence. If a subsequent hip fracture results in a hospital stay of two nights or more, the fracture would not be adjudicated (i.e., *Form 123 – Report of Fracture Outcome* would not be completed), but the hospitalization would require completion of *Form 125 – Summary of Hospitalization Diagnosis*. A subsequent report of a hip fracture where the hospital stay is only one night is not investigated in the WHI Extension Study.

8.10.3 Identification of Fractures from Medical Records, Discovery

Occasionally, a hip fracture not reported by the participant will be identified from medical records obtained while investigating other outcomes. When a hip fracture is identified in this manner, the Physician Adjudicator should return the case and request investigation of the fracture(s). The Outcomes Coordinator (OC) should investigate the outcome and obtain the required supporting documentation.

8.10.4 Form 123 – Report of Fracture Outcome

Administrative Questions

Date Completed: Date the Physician Adjudicator completed the form.

Adjudicator Code: 5-digit ID for the Physician Adjudicator.

Central Case No.: Case number assigned by WHIX.

Case Copy No.: Copy number assigned by WHIX.

Qx. 1 – Confirmed hip fracture

Radiographically-confirmed fractures of the proximal femur, including fractures of the femoral neck, intertrochanteric region, greater trochanter, and hip fracture – site not specified. Fractures of the subtrochanteric region are not included as proximal femur fractures.

The report must meet the following criteria:

- One or more of the following phrases must appear in the report: "fracture," "definite fracture," "break," "hairline fracture," "stress fracture," or "healing fracture."
- **And** the confirmatory report does not contain any of the following phrases: "possible fracture," "suspicious fracture," "probable fracture," "suspected fracture," or similar language indicating the diagnosis of fracture is "**uncertain**."

Situations where the Fracture Adjudicator needs to request more documents:

a) If the preoperative X-ray report indicates a hip fracture, and the X-ray was not evaluated by a radiologist, or if the radiology report is missing, the Fracture Adjudicator may confirm the fracture by review of X-ray reports or other documentation such as the operative or other orthopedist reports.

b) If the radiologist's report from a preoperative hip radiograph is negative or equivocal ("uncertain") but the hospital discharge summary indicates a proximal femur fracture, then the Fracture Adjudicator needs to request a written radiologist's report of either a bone scan, MRI, or CT scan that unequivocally describes the presence of a new, acute, or healing fracture of a proximal femur before confirming the hip fracture.

c) If the radiologist's report from a preoperative hip radiograph is equivocal ("uncertain"), or if the radiology report is missing, the Fracture Adjudicator needs to request a copy of the preoperative X-ray and other imaging studies, radiology reports, or clinical findings from the hospital record before confirming the hip fracture.

Qx. 1.1 – Date of diagnosis

Date of hospital admission for radiology confirmation of the hip fracture or the date of radiologic confirmation if no hospitalization occurred.

Qx. 1.2 – Fracture site

Base the fracture site for confirmed hip fractures on the information provided in the X-ray report. Refer to *Figure 8.9 – Fractures of the Hip*.

- In instances where fractures extend from one location to another (as defined on *Form 123*), for example, an intertrochanteric/subtrochanteric fracture, the first location mentioned in the radiology report will be considered the primary fracture site.
- In instances where the usual documentation (hospital discharge summary, operative report and radiology report), do not agree on the fracture location, final determination will be based on radiology report. In the case of equivocal radiology report, the Fracture Adjudicator may review the available films to make a final determination or request the Fracture Committee review the case

Qx. 1.3 – Side of hip fracture

Mark one: Right, left, both sides, unknown.

Qx. 1.4 – Hip fracture based on

Criteria used for diagnosis. The items are arranged in hierarchical order from the strongest to the weakest evidence of hip fracture. Mark the one category that applies best.

- Written report of hip fracture by a radiologist based on a preoperative radiograph and documenting the presence of a new, acute, or healing fracture of the proximal femur (or one of its regions: the femoral neck or intertrochanteric region). Fracture confirmation may include a written report not by a radiologist and based on a review of a radiograph, if the Fracture Adjudicator deems it appropriate (code 1).
- Radiologist's report confirms a proximal femur fracture, but the hospital discharge summary does not (or is equivocal or missing). The X-ray report alone confirms a proximal femur fracture (code 2).
- All of the following (code 3):
  1) Hospital discharge summary listing fracture of the proximal femur, femoral neck fracture, intertrochanteric fracture, trochanteric fracture, or hip fracture; and
  2) An equivocal written radiology report of the hip (e.g., "possible," "probable," or "suspected" hip fracture); and
  3) a written radiologist's report of either a bone scan or MRI scan unequivocally stating that a new hip fracture or healing hip fracture is present
- Hip fracture diagnosed in discharge summary, or other written report, but no radiology report available or radiograph not read by radiologist. This includes a hospital discharge summary or face sheet listing fracture of the proximal femur, femoral neck, intertrochanteric region or hip (code 4).

Qx. 1.5 – Pathologic hip fracture

Pathologic hip fractures are adjudicated, though they will be excluded from the primary fracture endpoint.

Pathologic Hip Fractures: Those resulting from anatomic compromise due to bone tumors, Paget's disease, bone and joint prosthesis, or surgical manipulation. Confirmation is obtained from the preoperative radiograph and/or the radiologic and operative reports. An osteoporotic fracture is not considered a pathologic fracture.

Mark "No" if the fracture occurred as a result of trauma sufficient to cause a fracture in normal healthy bone (e.g., a fall from a height or a motor vehicle accident) and no underlying bone abnormality was noted.

Mark "Yes" if the fracture was associated with a documented underlying bone abnormality or anatomic compromise related to bone tumor, bone cyst, Paget's disease (of bone), cancer metastasis, bone or joint prostheses, occurred at a pre-existing hip replacement site, or surgical manipulation. When present, these conditions are usually evident on the preoperative radiograph, and are noted in the radiologic report and the operative report. For example, a typical radiologic report will note "fracture of proximal femur adjacent to lytic lesions consistent with tumor. Cannot rule out underlying metastatic lesions." For fractures due to bone tumors, confirmation is usually available from a pathology report. Read the radiologic, operative, and pathology reports carefully for indications of pathologic fracture. However, these will be rare (< 2% of hip fractures).

- Periprosthetic fractures will be the most common type of pathologic hip fracture.
- An osteoporotic fracture is not considered a pathologic fracture.

Mark "Possible" if the incident leading to the fracture does not seem sufficient to cause a fracture in normal healthy bone, but there is no unequivocal evidence of an underlying bone abnormality. Fractures of the proximal femur during or subsequent to hip replacement procedures are coded as pathologic hip fractures and the location coded as "Unspecified Part of the Proximal Femur".

Responsible Adjudicator Signature

The Physician Adjudicator should sign the form only when s/he is satisfied that the questions on the hip fracture outcomes being reported have been filled in as completely and accurately as possible on the basis of all available information, and that other outcomes (e.g., hospitalization) have been investigated and adjudicated.

Figure 8.8
Form 123 - Report of Fracture Outcome

WHI **Form 123 - Report of Fracture Outcome** **Ver. 8.1**

OMB #0925-0414 Exp: 5/09

COMMENTS	-Affix label here- Member ID: __ __ __ - __ __ __ __ - __
To be completed by Physician Adjudicator: Date Completed: __-__-__ (M/D/Y) Adjudicator Code: __-__	Central Case No.: __ __ __ __ __ Case Copy No.: __

Use a separate form for each fracture.

Yes ☐1 No ☐0

1. **Confirmed hip fracture:** Fracture of the proximal femur, including fractures of the femoral neck, intertrochanteric region, and greater trochanter

1.1. Date of Diagnosis: __ - __ - __ (M/D/Y)

1.2. Fracture site: (***Mark the one that applies best.***)

☐1 Neck of femur (transcervical, cervical) ☐3 Greater trochanter
☐2 Intertrochanteric fracture ☐4 Unspecified part of proximal femur

1.3. Side of hip fracture: (***Mark the one that applies best.***)

☐1 Right ☐3 Both sides
☐2 Left ☐9 Unknown

1.4. Hip fracture based on: (***Mark the one category that applies best.***)

☐1 Written radiology report that is read by a radiologist and identifies the presence of a new, acute, or healing fracture of the proximal femur (femoral neck, intertrochanteric region, or the greater trochanter region) and documented on a discharge summary

☐2 Radiologist's report confirms a proximal femur fracture, but the hospital discharge summary does not (or is equivocal or missing)

☐3 All of the following:
1) hospital discharge summary listing fracture of the proximal femur, femoral neck fracture, intertrochanteric fracture, trochanteric fracture, or hip fracture;
2) equivocal written radiology report of the hip (e.g., "possible" or "probably" or "suspected" hip fracture); and,
3) a written radiologist's report of either a bone scan or MRI scan unequivocally stating that a new hip fracture or healing hip fracture is present

☐4 Hip fracture diagnosed in discharge summary, or other written report, but no radiology report available or radiograph not read by radiologist

1.5. Pathologic hip fracture: fracture resulting from bone tumors or cysts, Paget's disease, bone or joint prostheses, or surgical manipulation. Osteoporotic fracture is not considered a pathologic fracture. (***Mark the one category that applies best.***)

☐0 No ☐1 Yes ☐2 Possible

_____
Responsible Adjudicator Signature

RV_____K_____V_____

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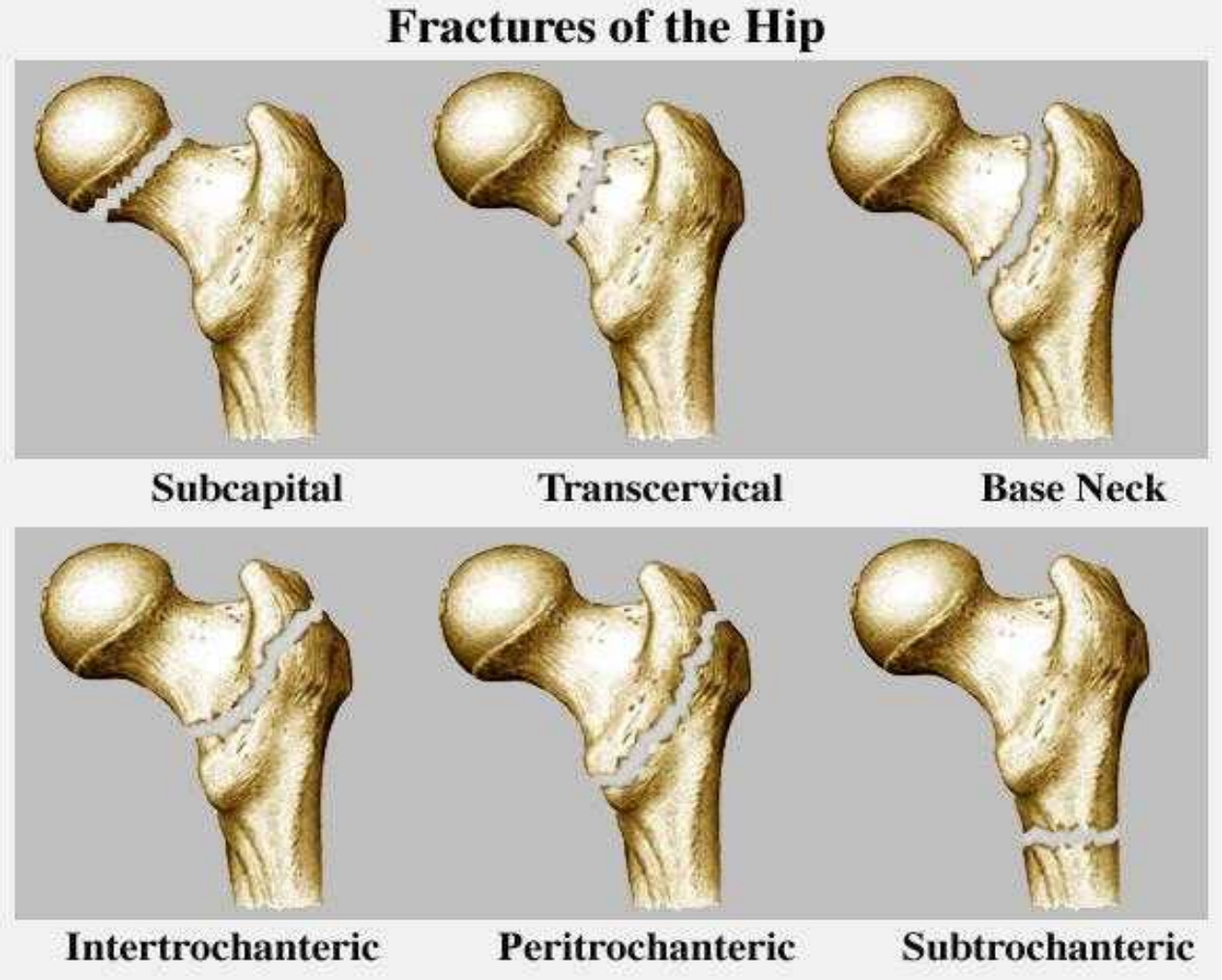
Figure 8.9
Fracture of Hip Views



8.11 Form 130 – Report of Cancer Outcome

The CCC Outcomes staff places the participant's barcode ID label in the space provided at the top of the form and routes the *Form 130 – Report of Cancer Outcome* and a copy of the supporting documents to the Cancer Adjudicator.

Administrative Questions

Date Completed: Date the Cancer Adjudicator completed the form.

Adjudicator Code: 3-digit ID for the Cancer Adjudicator

Central Case No.: Case number assigned by WHIX

Case Copy No.: Copy number assigned by WHIX

Qx. 1 – Date of Diagnosis

Date of diagnosis is a required field and must be completed. Record the date of the first tissue diagnosis for a new cancer. Generally, the first tissue diagnosis will be when the initial biopsy of the cancer is done. If no tissue was obtained to make the diagnosis, use the date of the first cytology diagnosis.

Tips for Date of Diagnosis:

- Oftentimes for leukemia cases, the first diagnosis may be made with a peripheral blood smear.
- Do not code '99 – Unknown' for day, month, or year of diagnosis. Currently, July is used as the default month and the 15th as the default day. If the year of diagnosis is unknown, use the best approximation.

Qx. 2 – Primary Cancer Site

Mark one primary cancer site. If a case has multiple cancer sites, complete a *Form 130* for each cancer site.

The primary cancer site is the applicable organ or tissue site where the cancer originated. This question lists the 'Main WHI Cancer Outcomes' sites separate from the 'Other Cancer Outcomes' sites.

If the primary cancer site is not listed under 'Other Cancer Outcomes' or is an unknown site, mark 'Box 00 - Other' and hand write the site or indicate 'unknown' in the space provided.

Tips for Primary Cancer Site:

- For the 'Main WHI Cancer Outcomes', breast only, complete the required questions, Qx.1-3 and Qx.5-14.
- For the other 'Main WHI Cancer Outcomes' (ovary, corpus uteri/endometrium, colon, rectum, rectosigmoid/rectosigmoid junction), complete the required questions, Qx.1-3 and Qx.5-10.
- For the 'Other Cancer Outcomes', complete the required questions, Qxs.1-6, to capture the fact of cancer. Note: Extension Study goal is to apply SEER coding to all 'Other Cancer Outcomes' sites for WHI and Extension Study primary sites.
- If the primary cancer site is listed under 'Other Cancer Outcomes', check the box provided in Qx.2 but do not enter a site code for Qx.3.
- Do not code primary cancer site as the secondary or metastatic site of the cancer.
- If 'Box 00 - Other' is marked, a corresponding ICD-0-2 (International Classification of Diseases for Oncology, Second Edition) must be entered in Qx3.
- Refer to *Form 130* for the list of the 'Main WHI Cancer Outcomes' and the 'Other Cancer Outcomes'.

Qx. 3 – ICD-0-2

A numeric ICD-0-2 code is recorded for the primary cancer site indicated in Qx. 2 for the 'Main WHI Cancer Outcomes' sites and those primary sites handwritten in the 'specify' field for 'Box 00 – Other'.

Qx. 4 – Tumor Behavior

This item is completed only when a primary site list under 'Other Cancer Outcomes' in Qx. 2 is checked.

Select one and only one category to classify the behavior of the tumor.

- Invasive; malignant; infiltrating; micro-invasive (code 1)
- In-situ, intraepithelial; non-infiltrating; non-invasive; intraductal (code 2)
- Borderline malignancy; low malignant potential; uncertain whether benign or malignant; indeterminate malignancy (code 3)
- Unknown (code 9)

Tips for Tumor Behavior:

- Code '3' is only used for ovary.

Qx. 5 – Reporting Source

This is a hierarchical field, lower numbers (e.g., code 1) take precedence over higher numbers. Select the first applicable category.

- Hospital inpatient (code 1)
- Hospital outpatient/radiation or chemotherapy facility, surgical center, or clinic (code 2)
- Laboratory only (hospital or private) including pathology office (code 3)
- Physician's office/private medical practitioner (code 4)
- Nursing/convalescent home/hospice (code 5)
- Autopsy only (code 6)
- Death certificate only (code 7)

Qx. 6 – Diagnostic Confirmation Status

This item indicates the nature of the best evidence available on the diagnostic confirmation of the cancer. This is a hierarchical field, lower numbers (e.g., code 1) take precedence over higher numbers. Select the first applicable category under the 3 headings '(Microscopically Confirmed', 'Not Microscopically Confirmed', 'Confirmation Unknown').

Microscopically Confirmed:

- Positive histology (pathology) (code 1)
- Positive exfoliative cytology, no positive histology (code 2)
- Positive histology (pathology), regional or distant metastatic site only (code 3)
- Positive microscopic confirmation, method not specified (code 4)

Not Microscopically Confirmed:

- Positive laboratory test/marker study (code 5)
- Direct visualization without microscopic confirmation (code 6)
- Radiography and other imaging techniques without microscopic confirmation (code 7)
- Clinical diagnosis only (other than 5, 6, or 7 above) (code 8)

Confirmation Unknown:

- Unknown if microscopically confirmed (code 9)

Qx. 7 – Laterality

Mark the one laterality that is applicable for the primary site.

- Not a paired site (code 0)
- Right: origin of primary (code 1)
- Left: origin of primary (code 2)
- Only one side involved, right or left origin unspecified (code 3)
- Bilateral involvement, lateral origin unknown: stated to be single primary (code 4)
- Paired site, but no information concerning laterality; midline tumor (code 5)

Qx. 8 – Morphology

The morphology code is a 6-digit code that includes the 4 digits of a common root code for a particular cell type, the 5th digit indicating the behavior code, and the 6th digit indicating the grading and/or differentiation of the cancer. The morphology coding for this field is from the ICD-O-2

Example: A malignant poorly differentiated adenocarcinoma is coded as 814033:

- Root code: 8140 - adenocarcinoma
- Behavior code: 3 - malignant
- Grade: 3 - poorly differentiated

Qx. 9 – EOD (SEER)

The EOD (extent of disease) is an estimate of the extent of disease based on all the evidence available during the first couse of treatment (4 months from date of diagnosis), in addition to the strictly clinical impression and any other evidence derived from the complete work-up of the participant. The coding for these EOD fields is site-specific.

The coding for EOD is broken into the following categories:

- Qx.9.1 – size of primary tumor
- Qx.9.2 – extension of tumor
- Qx.9.3 – lymph node status
- Qx.9.4 – number of regional nodes positive
- Qx.9.5 – number of regional nodes examined

Tips for EOD:

- Refer to appropriate SEER coding scheme for details of the codes.

Qx. 10 – Summary Stage (SEER)

The summary stage is the grouping of cases with similar prognoses into broad extent of disease categories, e.g., in-situ, localized, regional, distant, and unknown spread. The staging is done in accordance with the SEER site-specific summary staging schemes.

After the review of all evidence, mark the one appropriate stage of disease:

- In-situ (code 1)
- Localized (code 2)
- Regional (code 3)
- Distant (code 4)
- Unknown (code 9)

Questions 11-14 are completed for breast cancer only.

Qx. 11 – Complete the subclassification for Breast Histology 8522

Mark the one subclassification for the histology code 8522 – infiltrating duct and lobular carcinoma.

- Not applicable (code 0)
- Ductal in-situ plus lobular in-situ (code 1)
- Ductal invasive plus lobular in-situ (code 2)
- Ductal invasive plus lobular invasive (code 3)
- Lobular invasive plus ductal in-situ (code 4)
- Invasive cancer, ductal and lobular NOS (code 5)

Qx. 12 – Estrogen Receptor Assay

Mark the one category to indicate the result of the Estrogen Receptor Assay (ERA), if it was ordered but the results are not available, or if it is unknown if done or not done.

- Positive (code 1)
- Negative (code 2)
- Borderline (code 3)
- Ordered/Results not available (code 4)
- Unknown/Not done (code 5)

Qx.12.1 – Date

Indicate the date the tissue was excised (that was used for the ERA).

Qx. 12.2 – Type of Assay

Mark the one category to indicate the type of ERA that was done.

- fmol/mg protein (code 1)
- ICC/IHC (code 2)
- Other, specify (code 8)
- Unknown (code 9)

Qx.13 – Progesterone Receptor Assay

Mark the one category to indicate the result of the Progesterone Receptor Assay (PRA), if it was ordered but the results are not available, or if it is unknown if done or not done.

- Positive (code 1)
- Negative (code 2)
- Borderline (code 3)
- Ordered/Results not available (code 4)
- Unknown/Not done (code 5)

Qx. 13.1 – Date

Indicate the date the tissue was excised (that was used for the PRA).

Qx. 13.2 – Type of Assay

Mark the one category to indicate the type of PRA that was done.

- fmol/mg protein (code 1)
- ICC/IHC (code 2)
- Other, specify (code 8)
- Unknown (code 9)

Qx. 14 – Her 2/Neu

Mark the one category to indicate the result of the Her 2/Neu, or that it was not done or unknown if done.

- Positive (code 1)
- Negative (code 2)
- Borderline (code 3)
- Ordered/Results not available (code 4)
- Unknown/Not done (code 5)

Qx. 14.1 – Date

Indicate the date the tissue was excised (that was used for the Her 2/Neu).

Tips for ERA/PRA/Her 2/Neu Assays:

- The ERA/PRA/Her 2/Neu assays are generally done on an invasive tumor.
- Do not code the assay results if the tissue that was submitted was either lymph nodes or metastatic sites.
- Code assay results from the primary site tissue.
- A FISH assay will overide the Her 2/Neu since it will provide a more specific result.
- If Qxs 12, 13, or 14 are coded '9-unknown/not done', do not code 12.1, 12.2, 13.1, 13.2 or 14.1, respectively.

Figure 8.10
Form 130 – Report of Cancer Outcome

WHI **Form 130 – Report of Cancer Outcome** **Ver. 8.2**

OMB #0925-0414 Exp: 5/09

COMMENTS	- Affix label here- Member ID: __ __ __ __ - __ __ __ __ __ - __ #__
To be completed by CCC Cancer Coder: Date Completed: ___-___-___ (MM/DD/YY) Adjudicator Code: ___-___	Central Case No.: _____ Case Copy No.: ___

Use a separate form for each new diagnosis.

1. Date of Diagnosis: ___-___-___ (MM/DD/YY)

2. Primary cancer site: ***(Mark the one that applies best.)***

Main WHI Cancer Outcomes

- ☐ 50 Breast → **Questions 1–3, 5–14 required.**
- ☐ 56 Ovary
- ☐ 54 Corpus uteri, endometrium
- ☐ 18 Colon (excludes appendix, see below)
- ☐ 20 Rectum
- ☐ 19 Rectosigmoid junction

→ **Questions 1–3, 5–10 required.**

Other Cancer Outcomes → **Questions 1–6 required.**

- ☐ 31 Accessory sinuses
- ☐ 74 Adrenal gland
- ☐ 21 Anus
- ☐ 86* Appendix
- ☐ 24 Biliary tract, parts of [other/unspecified]
- ☐ 67 Bladder
- ☐ 40 Bones, joints & articular cartilage of limbs
- ☐ 41 Bones, joints & articular cartilage [other/unspecified]
- ☐ 71 Brain
- ☐ 72 Central Nervous System (excludes brain)
- ☐ 53 Cervix
- ☐ 49 Connective, subcutaneous & other soft tissues
- ☐ 75 Endocrine glands & related structures [other/unspecified]
- ☐ 15 Esophagus
- ☐ 69 Eye and adnexa
- ☐ 57 Genital organs, female [other/unspecified]
- ☐ 64 Kidney
- ☐ 32 Larynx
- ☐ 42 Leukemia [hematopoietic & reticuloendothelial systems [includes blood; excludes multiple myeloma]
- ☐ 22 Liver
- ☐ 34 Lung (bronchus)
- ☐ 77 Lymph nodes
- ☐ 83* Lymphoma, Hodgkin's disease
- ☐ 82* Lymphoma, non-Hodgkin's disease
- ☐ 44 Melanoma of the skin
- ☐ 85* Multiple myeloma
- ☐ 06 Oral (mouth) [other/unspecified]
- ☐ 05 Palate
- ☐ 25 Pancreas
- ☐ 07 Parotid gland (Stensen's duct)
- ☐ 47 Peripheral nerves & autonomic nervous system
- ☐ 12 Pyriform sinus
- ☐ 39 Respiratory system and intrathoracic organs [other/unspecified]
- ☐ 08 Salivary glands, major [other/unspecified]
- ☐ 16 Stomach
- ☐ 73 Thyroid
- ☐ 02 Tongue, part of [other/unspecified]
- ☐ 68 Urinary organs [other/unspecified]
- ☐ 55 Uterus, not otherwise specified
- ☐ 00 Other ***(Specify site. Enter site code in Qx. 3.)*** _____

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Figure 8.10 (continued)
Form 130 – Report of Cancer Outcome

WHI **Form 130 – Report of Cancer Outcome** **Ver. 8.2**

3. ICD-0-2 Code: **Complete for Main Cancer site or "Other Cancer" site not already specified in Question 2. (Note to ancillary study coder, complete as requested by CCC.)**

☐☐☐.☐

4. Tumor Behavior: **Complete only for an "Other Cancer" diagnosis.** ***(Mark one only.)***

☐ 1 Invasive; malignant; infiltrating; micro-invasive

☐ 2 In situ; intraepithelial; non-infiltrating; non-invasive; intraductal

☐ 3 Borderline malignancy; low malignant potential; uncertain whether benign or malignant; indeterminate malignancy

☐ 9 Unknown

5. Reporting Source: ***(Mark one only. If more than one category applies, mark the first applicable category.)***

☐ 1 Hospital inpatient

☐ 2 Hospital outpatient/radiation or chemotherapy facility, surgical center, or clinic

☐ 3 Laboratory only (hospital or private) including pathology office

☐ 4 Physician's office/private medical practitioner

☐ 5 Nursing/convalescent home/hospice

☐ 6 Autopsy only

☐ 7 Death certificate only

6. Diagnostic Confirmation Status: ***(Mark one only. If more than one category applies, mark the first applicable category.)***

Microscopically Confirmed:

☐ 1 Positive histology (pathology)

☐ 2 Positive exfoliative cytology, no positive histology

☐ 3 Positive histology (pathology), regional or distant metastatic site only

☐ 4 Positive microscopic confirmation, method not specified

Not Microscopically Confirmed:

☐ 5 Positive laboratory test/marker study

☐ 6 Direct visualization without microscopic confirmation

☐ 7 Radiography and other imaging techniques without microscopic confirmation

☐ 8 Clinical diagnosis only (other than 5, 6 or 7 above)

Confirmation Unknown:

☐ 9 Unknown if microscopically confirmed

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Figure 8.10 (continued)
Form 130 – Report of Cancer Outcome

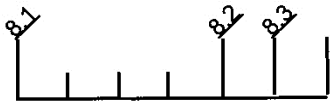
WHI **Form 130 – Report of Cancer Outcome** **Ver. 8.2**

Complete Questions 7–10 for Main Cancer Outcomes only.

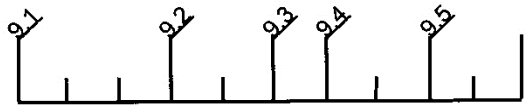
7. Laterality: ***(Mark one only.)***

- ☐ 0 Not a paired site
- ☐ 1 Right: origin of primary
- ☐ 2 Left: origin of primary
- ☐ 3 Only one side involved, right or left origin unspecified
- ☐ 4 Bilateral involvement, lateral origin unknown: stated to be single primary
- ☐ 5 Paired site, but no information concerning laterality; midline tumor

8. Morphology:



9. EOD (SEER):



10. Summary Stage (SEER): ***(Mark one only.)***

- ☐ 1 In situ
- ☐ 2 Localized
- ☐ 3 Regional
- ☐ 4 Distant
- ☐ 9 Unknown

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Figure 8.10 (continued)
Form 130 – Report of Cancer Outcome

WHI **Form 130 – Report of Cancer Outcome** **Ver. 8.2**

Complete Questions 11–14 for Breast Cancer Only.

11. Complete the subclassification for Breast Histology 8522: ***(Mark one only.)***

- ☐ 0 Not applicable
- ☐ 1 Ductal in situ plus lobular in situ
- ☐ 2 Ductal invasive plus lobular in situ
- ☐ 3 Ductal invasive plus lobular invasive
- ☐ 4 Lobular invasive plus ductal in situ
- ☐ 5 Invasive cancer, ductal and lobular nos

12. Estrogen Receptor Assay: ***(Mark one only.)***

- ☐ 1 Positive
- ☐ 2 Negative
- ☐ 3 Borderline
- ☐ 8 Ordered/Results not available
- ☐ 9 Unknown/Not done

12.1. Date: __-__-__ (MM/DD/YY)

12.2. Type of assay: **(Mark one only.)**

- ☐ 1 fmol/mg protein
- ☐ 2 ICC/IHC
- ☐ 8 Other:_____
- ☐ 9 Unknown

13. Progesterone Receptor Assay: ***(Mark one only.)***

- ☐ 1 Positive
- ☐ 2 Negative
- ☐ 3 Borderline
- ☐ 8 Ordered/Results not available
- ☐ 9 Unknown/Not done

13.1. Date: __-__-__ (MM/DD/YY)

13.2. Type of assay: **(Mark one only.)**

- ☐ 1 fmol/mg protein
- ☐ 2 ICC/IHC
- ☐ 8 Other:_____
- ☐ 9 Unknown

14. Her 2/Neu: ***(Mark one only.)***

- ☐ 1 Positive
- ☐ 2 Negative
- ☐ 3 Borderline
- ☐ 8 Ordered/Results not available
- ☐ 9 Unknown/Not done

14.1. Date: __-__-__ (MM/DD/YY)

_____
Coder Signature

15. Editor Code: __

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